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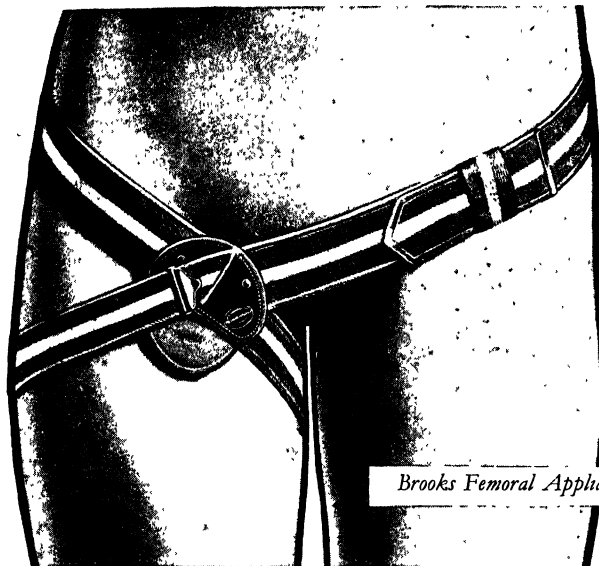
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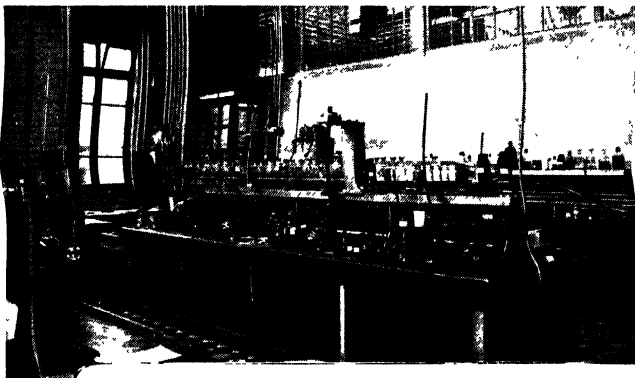
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INTRODUCTION

BY

THE GENERAL EDITOR

In this volume the text has been divided into three parts, which contain respectively a series of critical surveys of various fields of *medicine*, a discussion on some modern drugs, and abstracts from current medical literature.

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In this section an outline is given of recent advances in pharmaceutical knowledge and of the application of these to therapeutics generally.

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This section is designed to complete the picture with regard to the latest work on the subject of medicine generally. In view of the vast and increasing amount of experimental and clinical research which is being pursued in modern times, the difficulties of presenting a fully comprehensive account of this work are very considerable, but, by careful selection from current medical literature, British, American, and foreign, every effort has been made to overcome them and to present the most important information in the form of abstracts arranged as far as possible on the same plan as that adopted in the parent Encyclopaedia. Although the material in this part is intended to cover the various results and opinions recorded, it does not follow that they all will finally be accepted by the medical profession.

H. R.

PART I
CRITICAL SURVEYS

THE STATE AND NATIONAL HEALTH

BY SIR ARTHUR MACNALTY, K.C.B., K.H.P., D.M., F.R.C.P.
CHIEF MEDICAL OFFICER OF THE MINISTRY OF HEALTH, LONDON

INTRODUCTION

It must have been early in man's history that use was made of medical knowledge for the service of the community as well as of the individual.

It arose from circumstances similar to those which led to organized government. As soon as men began to live in tribes, in villages, and in communities, civil laws became necessary to punish crimes against person and property, and to maintain just dealing. Furthermore, from time to time plagues and diseases ravaged the community, and it was soon noticed that these were more intense and fatal when they were associated with filth, insanitary surroundings, and lack of proper medical treatment. The book of Leviticus, for example, is a compendium of early sanitary law. Moses enforced compulsory notification of certain diseases, and set out in detail systems of isolation and of disinfection of patients and of their dwellings. Pestilence has always been a stimulus to Public Health. In this country leprosy brought about the establishment of leper hospitals by the ecclesiastical authorities, and the beginnings of our present hospital system and of our method of notification and isolation. Plague indicated the necessity of sanitation in the hovels of the poor. The first Sanitary Act was passed by the English Parliament at Cambridge in 1388; it was followed by quarantine laws, by the appointment of scavengers, by sanitary watchmen, and by penalties for the concealment of infected persons. From mediaeval times the City of London has been a pioneer in sanitary reform, and many were the edicts promulgated by the Lord Mayor and the City Council for maintaining the health of the City, especially in times of plague and pestilence.

In another field, that of the Poor Law, the State had to make itself responsible for the relief of destitution and disease. The great monastic orders maintained in mediaeval England an extensive system of social relief. They had hospitals and asylums, and gave alms to the vagrant poor. The dissolution of the monasteries by Henry VIII created a vast social problem of destitution, which was dealt with by the first English Poor Law Acts of Elizabeth (1601). Poor rates, overseers, and houses for the sick and infirm were made by these Acts. Workhouses were established in 1722, and Poor Law Unions were formed by Gilbert's Act in 1782.

THE STIMULUS TO STATE MEDICINE THROUGH MEDICAL PROGRESS

It must be clearly understood that the State—though in times of stress and emergency highly appreciative of the advice and help of the medical profession—has never sought of its own initiative to impose a system of State Medicine upon the community. The pressure and impetus to this end have

come from without, in great part from the medical profession itself, and it is interesting to note how this has happened.

Greek medicine was active and progressive until it became doctrinal in Galen's interpretation of the Hippocratic writings. The Arabians disseminated Greek medicine to Western Europe. The teaching, intended to stimulate progress through the influence of Galen, paradoxically retarded it by its very authority, and it was not until after the Renaissance that a golden age of medicine began at Padua. In this country, William Harvey and John Hunter brought new vision and new learning into the healing art, and the Royal College of Physicians, and later the Royal College of Surgeons, set the high standards of professional knowledge and authority which have helped to make British medicine so pre-eminent.

MEDICAL CORPORATIONS CONSULTED BY GOVERNMENT

From time to time the College of Physicians was consulted, frequently concerning the practice of preventive medicine and the administration of public health measures, by the City of London, the Privy Council, and Parliament. In particular, the following activities of the College in relation to national health may be mentioned: they advised the Government on plague, on cholera, on influenza; they prepared the first and successive editions of the British Pharmacopoeia, until the Medical Act of 1858 transferred that duty from the College to the General Medical Council; they introduced Registration of the Cause of Death and official nomenclature of diseases; they petitioned Parliament in regard to the evils of excessive spirit-drinking, as a result of which Parliament passed the Gin Acts of 1736, 1751, and 1752 for the suppression of gin-shops and the restriction of private retail sales; for more than fifty years the College had control of the national movement for vaccination, inquired into its results, supervised the arrangements, and standardized and distributed the lymph. Subsequently, these duties were undertaken by the Privy Council from 1861 to 1871, by the Local Government Board from 1871 to 1919, and since that date by the Ministry of Health. Lastly, the Conjoint Board of the Royal Colleges in 1894 initiated work in the standardization, preparation, testing, and distribution to London hospitals of antitoxin for diphtheria.

But, in addition to the weight of authority and influence of these and other great medical corporations upon which the State relied and has continued to rely for advice in health matters, the fundamental clinical studies of communal disease by individual physicians brought their authoritative results to bear upon the question of national health. In the seventeenth century Glisson described rickets and Thomas Sydenham sought out general laws as to the prevalence and course of epidemic diseases.

PREVENTIVE MEDICINE IN THE EIGHTEENTH CENTURY

But it was in the eighteenth century, *par excellence*, that British practitioners of medicine laid the foundations of the administrative practice of modern preventive medicine. What a galaxy of medical constellations shines in that eighteenth-century firmament! Huxham investigated typhoid, typhus, Devonshire colic, scurvy, and diphtheria; Heberden, chicken-pox, rheumatism, measles, epidemic colds, and diphtheria; Fothergill, epidemic sore throat; Haygarth, smallpox and typhus; Pringle, gaol fever, dysentery, and influenza; Sir George Baker, Devonshire colic and scurvy; and Jenner, smallpox and cow-pox. Before the eighteenth century closed, two salient triumphs had been gained in the prevention of disease; smallpox had become controllable, and scurvy preventable through James Lind's discovery backed up by the adminis-

trative support of Blane and Pringle. The work of these men not only revealed that instructed administration could prevent or mitigate communal disease, but it reinforced the medical profession as a whole with fresh arguments and educated the public in the need of a national system of public health.

HEALTH ADMINISTRATION IN THE NINETEENTH CENTURY

They and their successors were happy in their occasion. From quarters other than medical the hour of need for State concern in national health was striking, as the wonderful nineteenth century dawned. The Reform Act of 1832 had given power to remedy long-standing abuses. The Factory Commission of 1833 had let light into the shocking conditions of children employed in the cotton trade. The Factory Act of 1833 limited the hours of work for children, and recognized the need for independent and impartial inspection by officials. A new and effective principle was thus introduced into the control of evils, whether of industry, of poverty, or of insanitation.

This Factory Act made a beginning in industrial reform, and the Poor Law Amendment Act of 1834 started modern legislation in preventive medicine. In 1842 public attention was aroused to the shockingly insanitary conditions under which the people lived by the Poor Law Commissioners' report on 'The Sanitary Condition of the Labouring Population of Great Britain'; this report was almost entirely the work of Sir Edwin Chadwick, their Secretary. In it Chadwick pointed out that the people could not be clean, because the water supplies were defective; that the annual loss of life by diseases induced by filth and bad ventilation was greater than the toll of lives exacted by modern warfare; that the physique of the younger population suffered from their bringing up in insanitary surroundings; that the effect upon the adult population was to make them short-lived, improvident, reckless, and intemperate; and that defective town-cleansing fostered habits of the utmost degradation. Then followed the Public Health Act of 1848, and the establishment of the General Board of Health, succeeded, first, by the Medical Department of the Privy Council, with Sir John Simon as chief medical officer, and, secondly, by the Local Government Board in 1871, of which the Ministry of Health is the successor.

Sir John Simon and his colleagues (Southwood Smith, Sir George Buchanan the elder, and others) made investigations into communal ill-health and disease and desirable remedial measures which were embodied in a series of blue-books and reports to the Privy Council. Preceding, or side by side with, these investigations, Thackrah had been inspired by the work of Bernardino Ramazzini, Professor of Medicine at Modena in the seventeenth century, to explore the particular effects of 'the principal arts, trades, and professions' on health and longevity as he witnessed them in the rapidly growing industrial city of Leeds; John Snow discovered that cholera was conveyed by polluted water; Michael Taylor of Penrith showed that typhoid fever and scarlet fever could be conveyed by milk; and William Budd, Murchison, and Sir William Jenner were elucidating many problems concerning fevers. All this wealth of medical knowledge was reinforced by 'the new humanity' and by the books of four novelists, Charles Dickens, Lord Beaconsfield, Charles Kingsley, and Mrs. Gaskell, who quickened the public conscience in regard to health and social abuses. Preventive medicine owes these writers a great debt of gratitude.

Yet the State moved slowly in those deliberate days, in spite of considerable dissatisfaction being expressed as to the lack of organization in public health and the disorderly state of the sanitary laws throughout the country generally. Once more the motive power came from without, and from a medical corporation. In May 1868, a Joint Committee appointed by the British Medical Association and the Social Science Association 'to promote a better

administration of the laws relating to registration, medico-legal inquiries, and the improvement of the public health' petitioned the Government for the appointment of a Royal Commission in relation to these objects. The results of this Commission were wide and far-reaching.

ESTABLISHMENT AND GROWTH OF LOCAL AUTHORITIES

In 1872 local authorities, such as urban district councils and rural district councils, were set up, and in 1875 the great Public Health Act—the *Magna Carta* of Public Health, as it has been termed—was passed by Disraeli's Government. This consolidated all the previous sanitary enactments into a great sanitary code. It confirmed an Act of 1872 making compulsory the appointment of Medical Officers of Health by local authorities; it aimed at securing the drainage of houses, the sewerage of towns, the scavenging of streets, the removal of house refuse, wholesome conditions within houses, and the isolation of infectious persons.

Mark the growth of local authorities—first the parish, then the urban or rural district, lastly, in 1888, the creation of County Councils on an elective basis with the formation of Counties and County Boroughs.

But it is only within recent times that the Counties and County Boroughs have attained their present supremacy as Guardians of the Public Health. The County Councils at first had limited Public Health powers. The districts remained, as they do to-day, the administrators of the Public Health Acts. The years 1875 to 1900 cover a long series of progressive reforms under the direction of the Local Government Board, which supervised especially such local government as related to the public health and the relief of the poor. These reforms comprise general sanitary improvements, pure water supplies, pure food supply, provision of isolation hospitals, public vaccination, and the supervision of slaughter-houses and common lodging-houses. Local authorities obtained control over housing, and powers to condemn slums and to provide new housing accommodation. Infectious diseases were made notifiable, and port sanitation prevented the admission of fresh disease, including plague and pestilence.

IMPROVEMENT IN THE NATIONAL HEALTH THROUGH ENVIRONMENTAL HYGIENE

One of the greatest boons during this period was the purity of the water supplies. For centuries English drinking-water had an unenviable reputation. In the fifteenth century Henry VII wrote to Ferdinand and Isabella to the effect that the water of England was undrinkable, and that therefore the young Princess Katherine of Aragon, betrothed to Prince Arthur, should be accustomed to drink wine. The water-borne diseases have become reducible. Cholera has been abolished among us, and typhoid fever is much less common. Personal cleanliness and lessened overcrowding have stamped out typhus, the deadly 'gaol-fever', which spread from the prisoner in the dock to the judge on the bench. No longer is every second person we meet scarred with smallpox. The general decline in mortality and the improvement in national health were indeed remarkable, when it is remembered that urbanization, a process favourable to the diffusion of infection, was on the increase.

During this period the emphasis was on environmental hygiene. Apart from the general establishment of isolation hospitals for infectious diseases, public medical services were, broadly, available only for the sick poor under the Poor Law; these services comprised the infirmaries provided in conjunction with the Poor Law institutions, and, for the home, the general

practitioners employed by the boards of guardians on a part-time basis as district Poor Law medical officers.

WIDENING SCOPE OF PREVENTIVE MEDICINE

The great advances made in medical and natural science contributed largely to administrative progress. For this was the age of Darwin, Huxley, and Lister, of Pasteur, Simpson, and Koch, and of Stephenson and Watt, in the fields of biology, antiseptic surgery, bacteriology, anaesthetics, and engineering science. The skill and experience of many branches of knowledge have been assembled to constitute the science of public health.

As medicine progressed, preventive medicine took a new orientation. Before bacteriology was known and applied, environmental conditions, defective plumbing, miasmas and the like were looked upon as responsible for much of the generation and propagation of disease. When the microbic aetiology of certain diseases was revealed, individual hygiene assumed a new importance for the public weal.

This new movement which has now come to fruition is based on recognition of the fact that the interest of the community calls not only for the removal of environmental conditions which favour disease, but, equally, for attention to personal hygiene, physical health, and nutrition, to the detection and treatment of disease in individuals in its early stages, and, indeed, to the general medical needs of those sections of the community which are not reasonably able to make provision for medical attention out of their own resources.

The succeeding trend of preventive medicine from the reign of King Edward VII onwards has therefore been in the direction of placing the individual in the best possible condition to resist disease, of checking disease at its onset in the individual, of preventing the personal transmission of disease in human beings, and thus diminishing the dosage of infection, and of curing or ameliorating declared disease. At the same time progress in environmental hygiene has not stood still. There has been a long series of Housing and Town Planning Acts, and factory legislation has steadily advanced.

Over and above all this, local authorities have the task of maintaining and extending sanitary amenities, water supplies, sewage and refuse disposal, and food control. Indeed, fresh strains have been thrown upon local authorities in these respects through the rapid increase of urbanization and new housing estates.

Preventive medicine has now enlarged its activities by taking the individual in hand, by promoting facilities and education for keeping him healthy, and by treating disease in the individual in order to safeguard the community. The State has done this in successive stages. The services have been planned independently to meet some pressing need, e.g. tuberculosis, and it is only in these latter days that they are being integrated and co-ordinated.

THE NATIONAL HEALTH SERVICES

The State made an important contribution to this wider interpretation of public health by instituting the School Medical Service in 1907 with the support and insistence of the medical profession. It is designed 'to improve the health conditions, both personal and in regard to environment, of the children of the nation' and to endeavour to secure 'the physical improvement, and as a natural corollary, the mental and moral improvement of coming generations'.

In successive reports of the chief medical officer of the Board of Education it has been shown how medical inspection of school children has separated the impaired and defective child from the normal and healthy, how arrangements

have been made for attending to the health of both sick and healthy children, how many morbid conditions have been reduced, how the general physique of school children has improved, and how, in addition to direct medical results, the teaching of hygiene and cleanliness, the physical training and the provision of school meals have reformed the physical condition of the children of this land beyond all comparison with the past. A health conscience has developed both in the children and in their parents.

The reign of King George V is remarkable for steady and rapid advances in preventive and curative medicine. These have gradually brought all agencies for promoting national health under closer and more helpful control. The tuberculosis work of local authorities includes both prevention and cure; in the child welfare and maternity services the clinician works side by side with the hygienist; maternity services have been developed by the Midwives Act of 1936, and by reports of the Ministry of Health on Maternal Mortality; and the insurance medical service is designed for the prevention as well as the treatment of disease, and is now working in closer relation with the public health services. Lastly, the Local Government Act of 1929 greatly increased the hospital resources of county and county borough councils, and provided for a more intensified co-operation between municipal and voluntary hospitals in a joint war against disease. Thereby the administrative responsibilities of county and county borough medical officers of health have been greatly augmented and extended. It is to be observed, also, that the establishment of the Ministry of Health by the passing of the Ministry of Health Act in 1919, has largely contributed to this wider outlook upon preventive medicine. The Ministry is now a central authority of comprehensive health services, which is interlinked and intimately co-ordinated not only with local authorities and the multiple health bodies of Great Britain, but through the Office International d'Hygiène Publique and the Health Committee of the League of Nations with the health services of the whole world. 'It aims at bringing every advance in medical science, every measure calculated to maintain health and to prevent disease to the service of the people, and to make health the birth-right of every inhabitant of this country.' The Ministry's influence in this respect is greatly strengthened by the ungrudging help and advice which the Minister receives, not only from other Government departments, including the Medical Research Council, but also from the representative bodies of the medical profession and a host of voluntary societies and associations concerned with various aspects of public health.

In recent years further conspicuous advances have been made in medical knowledge, and these, in turn, have enhanced the potentialities of preventive medicine. Mention may here be made of the wider recognition of deficiency diseases and the new and ever-increasing knowledge of vitamins. Closely associated is the successful treatment of pernicious anaemia by liver therapy. Still another biochemical triumph was the discovery in 1922 of insulin which revolutionized the treatment of diabetes mellitus, and the work on endocrines is opening out new lines of research. The study of chemistry of the blood has advanced the knowledge of metabolic disease. Fresh discoveries are recorded in neurology, psychiatry, heart disease, and many other branches of medicine. Orthopaedic surgery is preventing the onset of crippling, and treating cripples with new knowledge and new methods. Collapse therapy has achieved success in the treatment of pulmonary tuberculosis. In the most difficult problem of cancer important ground has been gained. Local authorities are co-operating with the Ministry of Health, the Radium Commission, the British Empire Cancer Campaign, and the voluntary hospitals in more adequate and wider measures; the Imperial Cancer Research Fund is organizing research on a more comprehensive scale; and radium and deep X-ray therapy are being increasingly employed. The Cancer Act of 1939 makes modern methods of treatment more generally available. The vital

importance of medical research has been recognized by the creation of the Medical Research Council, which has now more than twenty years of successful achievement to its credit.

SOME RESULTS

The rapid expansion of the national health services within a life-time is evidence of progress. It is true that people now lead healthier, more temperate, and more open-air lives. But the following changes in mortality in a quarter of a century may be attributed, at any rate in part, to the operation of public preventive and clinical services.

	1910	1937
(a) Infant mortality per 1,000 live births at ages		
0-1 years - - - - -	105	58
(i) Common infectious diseases - - -	7	2
(ii) Tuberculosis - - - - -	4	1
(iii) Diarrhoea and enteritis - - - -	13	5
(iv) Developmental and wasting diseases - -	40	28
(v) Other causes - - - - -	41	58
(b) Death-rates per million children living at ages 5-15	2,491	1,499
(c) Standardized death-rates per million from tuberculosis		
Respiratory - - - - -	988	523
Non-Respiratory - - - - -	434	134
(d) (i) Standardized death-rates per million from general paralysis of the insane		
Males - - - - -	94	22
Females - - - - -	24	8
(ii) Death-rates from syphilis per million at ages 0-5 years - - - - -	291	52
(e) (i) Standardized death-rates per million from typhoid fever - - - - -	53	5
(ii) Death-rates at ages under 15 per million living from		
Measles - - - - -	750	114
Scarlet fever - - - - -	200	31
Diphtheria - - - - -	384	310
Whooping-Cough - - - - -	798	195

These are remarkable and indeed amazing figures. They answer with no uncertain voice the question whether national expenditure on the provision of health services has been worth while.

ROLE OF THE MEDICAL PRACTITIONER IN STATE MEDICINE

The success achieved by British State Medicine is due to the fact that its organization has not been imposed arbitrarily from above, but it has developed gradually to meet public needs, and has always associated with itself all forms of voluntary effort, both medical and lay. As already observed, there have been disproportion and a certain amount of unnecessary overlapping and complication in such a planning. But the inconveniences, and sometimes unwieldiness, of the organization are fully compensated for by the good-will that cements its structure.

In particular reference must be made to the medical practitioner. He is

the foundation of a medical service, 'its pivot, its anchor, its instrument'. It must not be forgotten that many general practitioners are employed by the State either in a whole-time or in a part-time capacity, e.g. in the Ministry of Health, in the Post Office Service, the School Medical Service, the Public Assistance Medical Service, and so forth. There are 16,000 general practitioners employed in the National Health Insurance Service.

During the greater part of the nineteenth century, every qualified medical practitioner was regarded by the public as competent to deal with all branches of medicine, surgery, and obstetrics. In theory this remains true, but the wealth of new knowledge demanding in its branches individual study, technique, and constant application makes the general practitioner of to-day unwilling to undertake major operations or to pronounce the final opinions upon difficult problems of disease. Neither is it expected of him by his patients. This state of affairs for many years has been recognized by the National Health Insurance Service, which only requires insurance medical practitioners to render to insured persons medical services which are within the ordinary competency and sphere of a general medical practitioner.

The number of specialized services and pathological laboratory aids provided by local authorities enables the private practitioner to obtain for his patients specialized treatment, which he himself could not give.

But, in providing these services, the State has wisely done nothing to infringe the mutual confidence existing between doctor and patient. It is this mutual confidence which enables the doctor not only to treat the patient for declared ills, but also to advise him how to avoid them. From his knowledge of the individual patient the doctor is best fitted to prescribe for him rules of conduct, diet, and exercise, which are adaptable to his needs and capabilities. The practitioner can exert a great influence also for the common weal by familiarizing himself with the available health services, and by utilizing them for the benefit of his patients. He should be in close touch with the Medical Officer of Health and the Medical Officers of the local authority. They for their part should take full advantage of the practitioner's co-operation, and should keep him fully informed of the health services, including the aids to diagnosis and treatment, in his area. A wide knowledge of the health services needs also to be conveyed to the population generally, to the well to keep them fit, to the ailing in order that they may consult their doctor and take advantage of them. In this important matter of health education great assistance is being given to local authorities by such important bodies as the Central Council for Health Education, the British Social Hygiene Council, and the National Association for the Prevention of Tuberculosis. All these and similar agencies of repute enjoy the support of the Ministry of Health, the Board of Education, and the British Medical Association.

CONCLUSION

In these hundred years of organized work much has been achieved by the State for national health. While the encouraging side of the picture has been dwelt upon, much remains still to be done.

Diseases of the heart and circulation, cancer, pneumonia and other respiratory diseases, nervous diseases, and tuberculosis still exact too heavy a toll in our national bills of mortality, and too many infants still perish in the first year of life. Preventive medicine no longer is restricted to the comparatively simple task in a particular area of dealing with sanitary evils and disease, of improving individual and environmental hygiene, and of introducing the next generation to a better state of things. Populations are shifting, urbanization is increasing, and the internal combustion engine and modern methods of transport have accelerated the speed of life. The human machine, especially in adolescence, is often driven so hard that it

breaks down. Nervous collapses and mental disease give cause for anxiety and cannot be dissociated from modern conditions of life, while from time to time disease, baffled in one form, breaks out in another, as epidemic encephalitis has done.

Over and above these new difficulties and dangers, the health administrator has to consolidate the work done, and to keep the old and proved defences in repair, lest at any time the lurking enemy may make a breach in them. Nevertheless, through learning what has been already achieved, the outlook is one of confidence. Every year medical research forges new weapons and places them in the clinician's hand for the fight against disease. Each year the weapons are more keenly tempered and of greater potency. A great field of work lies open in the sociological side of medicine, such as the study and removal of those social conditions which promote ill-health, retard a patient's recovery, or favour his relapse.

The organization of British State Medicine is thus a comprehensive and responsible task. Its founders have realized that a national system of health must be supported by, and express the will of, the people, it must enlist all agencies, voluntary as well as official, under the national banner, and its planning must be sound and scientific. The success achieved by British State Medicine is due to the holding fast to these principles. Equally, they must inspire future advances in the subject.

GENERAL MEDICINE

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The present state of medical knowledge and the probable lines of advance in the immediate future can be appreciated only if the past is studied and directions of recent progress ascertained. In a subject so large it is natural that advances are taking place more quickly in some parts, while others are at a relative standstill, but the divisions of medical science and medical practice are so intimately related that new knowledge in one branch soon affects others and leads to improvements in the practice of all branches, with regard to both the prevention and treatment of disease. Advances in knowledge of the causes of disease lead to measures of prevention and cure, and, if such advances are rare, they influence the lives of men and the progress of mankind endlessly and in unforeseen ways. These are landmarks in medical science. Advances in knowledge of human physiology and of the reactions of the body to diseases are constantly taking place, with a better understanding of the significance of signs and symptoms and a clearer visualization of the way in which the body can be aided to return to health. Closely linked with these advances are improvements in therapeutic measures based on physical or dietetic methods or on the use of drugs which, though not curative, assist the natural tendencies to recovery and the adjustment of damaged organs and tissues to a greater state of efficiency. A consideration therefore of the directions in which the science and practice of medicine are advancing may conveniently be made under the following headings: (a) causes of disease; (b) prevention and treatment of disease; (c) mechanism of symptoms and symptomatic treatment.

CAUSES OF DISEASE

In spite of extensive and detailed knowledge of the clinical and epidemiological aspects of diseases that appear to be due to bacterial or other infections, efficient control cannot be exercised until the causal agents are known. In spite of the greatly increased knowledge of bacteria and their biological effects, the exact causes of many diseases considered to be due to infections with bacteria remain undiscovered. As methods of studying filterable viruses are being evolved, and as methods for their recognition and identification improve, more of these infective diseases are found to be caused by agents of this class. Benign lymphocytic meningitis and lymphogranuloma inguinale are now accepted as virus diseases, but of others, important because of their prevalence and the invalidity they produce, the causes are still unknown in spite of much organized research by all the new methods of investigation. Acute rheumatism, rheumatoid arthritis, mumps, influenza, and Hodgkin's disease are examples. There is evidence that viruses play some part in these conditions, but whether they are causal, partly causal, or only accidentally associated, is still unknown. The curious association of a virus with a bacterium in swine influenza suggests that both types of infecting agents may be necessary to produce disease. Important advances may be expected on these lines in the near future.

Pneumonia

Of the diseases due to bacteria, progress is occurring in details that are of the utmost importance for prevention and treatment. More exact analysis by methods based on immunology has shown that there are 32 types of pneumococci that cause lobar pneumonia, thus complicating the problem of aetiology, but at the same time clarifying the possibilities of treatment by immune sera.

The recognition of the very large number of types of streptococci has already great practical importance in relation both to immunotherapy and chemotherapy and should lead to still further progress. The recognition of the ineffectiveness of antibacterial sera compared with antitoxic sera has stimulated the search for soluble toxins as factors in the pathology of diseases due to bacteria. The erythrogenic toxin of the streptococcus of scarlet fever is a well-known example, and the recent work on meningococci is suggestive that a soluble toxin is important in the pathology of meningococcal meningitis and can be neutralized by an antitoxic serum.

Drug intoxications

The development of pharmacology in the nineteenth century, and the recognition of the poisonous effects of drugs, led to the conception of intoxications as the causes of disease and to a wide-spread search for antidotes. This toxæmia hypothesis is still held for many diseases of unknown cause, and the hypothesis of intrinsic toxins is a further development that has served as an unfortunate cloak for ignorance and an excuse for inefficient therapy. Recently, extrinsic intoxication has acquired a new importance in relation to the extensive development of synthetic drugs and of synthetic chemicals used in industry, and intrinsic intoxications may prove to be the mechanism of the production of some of the symptoms found in deficiency diseases. The production of agranulocytosis as the result of an idiosyncrasy to amidopyrine, the hepatitis and skin eruptions that follow the use of the arsphenamines, and the various, but fortunately rare, toxic effects of drugs of the sulphonamide group are examples of the former. Recognition of these effects at the earliest possible moment, and withdrawal of the drugs, are essential to avoid disasters, and doubtless modifications of chemical structure, or other means, will be found to enable the beneficial effects to be maintained and the deleterious to be eliminated.

More easily avoided by efficient official control are such intoxications as the neuritis due to tri-*ortho*-cresyl phosphate found in extract of ginger prepared in America in 1930, the wide-spread damage to the central nervous system caused by organic mercurial compounds such as methylmercuric iodide, used in industry, and the fatalities due to the use of diethylene glycol in an elixir of sulphanilamide.

The mechanism of the production of the symptoms in many of the deficiency diseases is still obscure, but the recent work on the results of deficiency of vitamin B₁ in altering the metabolism of carbohydrates and producing pyruvic acid, especially in the central nervous system, indicates how disease and ill-health may be due to poisonous substances formed in the body.

Dietetic deficiency diseases

Of the fields in which medical science is at present making significant progress, none is more full of possibilities and more likely to affect the practice of medicine than that of nutrition and the dietetic deficiencies. Although, apart from rickets, scurvy, beri-beri, and pellagra, known for some years to be deficiency diseases, it is not possible to point to any well-known disease of hitherto unknown cause and state that the cause has been recently shown to be due to a dietetic deficiency, yet the importance of dietetic factors in the growth of children is becoming more firmly established, and the chemical

identity of the factors is being elucidated. Tests are being devised to determine the presence of relative deficiencies, and the disappearance of symptoms following the administration of purified products is proving conclusively that vague symptoms of ill-health and certain symptoms hitherto regarded as complications of other conditions are clearly the result of deficiencies. The neuritis present in chronic alcoholism, in pregnancy, and in certain conditions of malnutrition is due to deficiency of vitamin B₁; certain forms of glossitis, dermatitis, and gastro-intestinal disturbance are due to deficiency of nicotinic acid; purpura and delayed healing of wounds are in some instances the result of deficiency of vitamin C; and maladaptation to dim light results from deficiency of vitamin A.

In cardiology important advances in the aetiology of heart disease appear probable. It is at times impossible to determine the cause of heart failure, and, as the clinical features of heart disease and heart failure due to vitamin B₁ deficiency are being defined and recognized, there seems little doubt that cases of heart failure occur from this cause quite apart from epidemics of beri-beri and in countries where such an aetiological factor in heart disease has not hitherto been suspected.

The significance of vitamin E in persistent miscarriage in human beings, likewise requires confirmation.

These advances in knowledge concerning the results of nutritional defects are of great importance because they have rendered the treatment simple, and they are most certainly of national and racial significance. That deficiencies are sometimes due not to actual deficiency of intake but are conditioned by factors governing absorption, utilization, and relative requirements is also established, and this widens the possibilities of their occurrence and increases the importance of considering them as possible aetiological factors in conditions regarded hitherto as unlikely to be associated with dietary deficiencies.

Endocrine diseases

So much work is being done, and so much progress made, in the sphere of internal secretory glands that there is a strong temptation to apply the results of laboratory work to diagnosis and treatment without justification. This is especially so since extracts derived from the anterior pituitary and the sex glands, or synthetic compounds closely allied in action to the active principles in such extracts, have powerful and interesting physiological and pharmacological properties. It is already clear that certain disturbances of sexual development, of the menstrual cycle, and of the menopause are due to the diminished production of hormones, and that the anterior pituitary reacts sensitively to any alteration in the hormonal balance, producing a seemingly compensatory excess of secretion with effects on other organs. Thus symptoms of excess of one hormone are frequently accompanied by symptoms of deficiency, or of excess, of others. This generalization has long been recognized in neoplastic diseases of the pituitary gland whether associated with excessive activity as in acromegaly or with diminished activity as in dystrophia adiposogenitalis, but the new knowledge of the actions of hormones due to the availability of purer products, and the development of methods for their assessment, indicate that many of the conditions hitherto considered as due to various combinations of excessive and diminished activity will shortly be analysed and clarified. So far little advance has been made in elucidating the cause of these disturbances in the absence of neoplasms.

For curative treatment or prevention to be developed it is not sufficient to note that a gland is atrophic or hyperplastic; the cause of these changes must be discovered. So far this knowledge is lacking, though the evidence of Sheehan that ischaemic necrosis of the anterior pituitary in varying degrees is the result of post-partum haemorrhage and other complications of labour is a step in this direction. It seems probable that progress in endocrinology will

soon result in knowledge of the causes of the extremely common less severe grades of endocrine disturbances that affect so profoundly the lives and social relations of individuals.

Degenerations

The advances in medical science made in recent years with the consequent improvements in methods of prevention and cure of disease have affected mainly the diseases of the younger age-periods, so that a greater proportion of the population is living to reach the older age-periods. The result has been that the diseases characteristic of the later periods of life are more prevalent. These are the result of degenerations in organs and tissues, of the causes of which little is known. They may be the effects of 'wear and tear', and since transport and communication have become quicker the pace of life has increased generally, so that increased 'wear and tear' may be a factor in their prevalence additional to that of increase in the average expectation of life. That these degenerations are inevitable must not, however, be taken for granted. That they are frequently the result of ischaemia is certain, but such a conclusion is merely a step towards discovering the cause, for the causes of vascular degenerations from which ischaemia results are unknown. The degenerative diseases are attracting more attention and their pathology and symptomatology are subjects of much investigation, so that progress in knowledge of their causes may materialize before long.

Mental diseases

Stimulated initially perhaps by the high incidence of psychoses and psychoneuroses during the Great War, during the post-war years there has been a progressively increasing interest in those diseases that result from psychic trauma or stresses. While it is possible that such conditions are now more prevalent, it is certain that more attention is being paid to them. The wiser physicians of the past always recognized the presence and the importance of psychic factors in ill-health, and in their wisdom and from their knowledge of men were able to treat such factors or were content to help their patients to adjust their lives more successfully in spite of them.

The tendency of recent years has been towards a more concise definition of these disturbances, and towards determining their origins so that curative treatment could be attempted by explanation, persuasion, and reassurance. The necessary investigations are time-consuming, and cases other than those in which the cause is simple and obvious have been entrusted to specialists. The high incidence of these conditions in general practice is producing from the medical profession a demand for instruction, so that only the more difficult cases need be referred to specialists. Such a demand for instruction from the medical profession and from the public necessitates the systematization and clarification of the subject and of the methods of investigation. Advances are taking place slowly along these lines.

Better opportunities are available for the psychological investigation of patients with minor degrees of the neuroses and also of cases of organic diseases with which psychological factors appear to be commonly associated. Faulty functioning of the organs controlled by the involuntary nervous system is often associated with psychic stress and is amenable to psychological treatment, and it is regarded by some that organic diseases, such as peptic ulcer and ulcerative colitis, may follow from faulty functioning of the organs concerned. The results of psychotherapy in such conditions are not sufficiently convincing to establish the causal relationship, and until we understand the mechanisms by which psychic stresses can produce disturbances in the functioning of organs and so result in organic disease, psychological causation of these organic diseases must be regarded as not established, for the psychological disturbances frequently encountered in these diseases may be associated

with the characteristic personality of these patients. It is obvious that advances of great importance in aetiology and curative treatment may develop in this field.

Minor ailments

The outstanding advances now being made towards the discovery of the causes of disease and ill-health appear to be concerned with minor ailments and the less severe or earlier disturbances of health. The newer knowledge of nutritional deficiencies, of the endocrines, of intoxications, and of medical psychology is in each instance providing evidence that is certainly suggestive and thus indicates the lines on which further investigation should be pursued. In dealing with conditions of this kind the proof that these minor maladies are caused by the above will be difficult to obtain, and must rest finally on their successful prevention and treatment in sufficient numbers to be conclusive, for concise and controlled experimentation and observations are difficult to devise. This new knowledge provides also the means of recognizing even earlier stages of disease before any symptoms or departure from health have become apparent, conditions that have been described as sub-clinical. The development of this field of medical science is clearly of great importance for the production and maintenance of a healthier, happier, and more efficient race.

PREVENTION AND TREATMENT OF DISEASE

As for various reasons the value of each individual to the State and to the race becomes greater, methods for ensuring better physical efficiency and for preventing disease are stressed and their importance recognized. The science of nutrition increasingly indicates how these objects may be attained, and shows how a well-balanced dietary is necessary for optimal growth during childhood and adolescence, and for protection against infections. The relationship of dietetics with economics and housing points to the necessity for the adoption of greater measures for obviating many preventable causes of ill-health and inefficiency.

Immunization in acute specific infections

Concerning the epidemic diseases such as diphtheria and scarlet fever, the practice of identifying susceptibles and of protecting them by active immunization spreads slowly, and the importance of carriers is being more widely recognized and the application of methods for their identification and isolation standardized. The toll on life and on health attending the wide-spread infection of measles is perhaps better checked by modification of the disease in the individual than by the temporary protection afforded by passive immunity, and the optimal method of effecting this by convalescent or adult serum is being determined. Similar methods for dealing with whooping-cough by vaccination are less advanced. Influenza continues to be a scourge and, although the term includes upper respiratory infections of varying aetiology, the isolation of a virus in certain human epidemics offers hope that the cause or causes of this dread infection will soon be discovered. Experiments on its control by vaccination with killed virus have not yet proceeded far enough to justify any confidence that it may be checked by this method.

The treatment of infections by passive immunity has been enriched by the addition of sera against the less common types of pneumococci that cause pneumonia, and by the standardization of antitoxic sera against the toxins of *B. oedematis* and of *Cl. septicum* as well as against the toxin of *Cl. welchii*; but the introduction of chemotherapy with sulphonamide drugs and the simplicity of this method of oral treatment has caused doubt as to the practical value of serum treatment of pneumonia, particularly in view of the labour and expense involved in the determination of types, and the disadvantages

of the intravenous administration of serum. It may well be established that serum treatment in conjunction with chemotherapy is more efficient than either alone, and that the combined method is necessary to save life in the more serious cases. The value of staphylococcus antitoxin in the treatment of staphylococcal septicaemia is not yet established, and further clinical trials on a large scale are required before the value of antityphoid serum as based on the work of Felix can be assessed.

Chemotherapy

The most notable developments in treatment are in chemotherapy. The introduction of the sulphonamide group of drugs for the treatment of infection by haemolytic streptococci has been followed by results that are dramatic, and by an extension of their usefulness as clinical trials take place and further chemical modifications in the compounds are devised. These compounds are effective by oral administration, rapid in their action, and remarkably free from toxic complications. They are bacteriostatic and not directly bactericidal; though they are strikingly effective, their limitations and dangers in the infections in which their usefulness has been demonstrated have yet to be fully defined. The pyridine compound usually called M & B 693 is at present the most universally effective and is the only one now used in the treatment of pneumonia, but it is possible that, as modifications of chemical composition are introduced, a greater specificity of action against bacteria will be found. The diseases in which the curative value of these compounds is accepted include puerperal sepsis, erysipelas and other infections with haemolytic streptococci, *Bact. coli* pyelitis, pneumonia due to pneumococci and to haemolytic streptococci, meningococcal meningitis, gonorrhoea, and lymphopathia venereum. Reports have also been published of their efficacy in brucellosis, but confirmation is still required. The response obtained in lymphopathia venereum is of interest because this disease is considered to be due to infection with a filtrable virus, and it is thus possible that a clue has been obtained that will lead to the control of a large number of important diseases due to viruses.

Endocrine therapy

Treatment by endocrine replacement is in a phase of regrettable and dangerous exploitation. The progress in knowledge of the part played by the sex hormones in health and in disease has been rapid, and the chemical identification and isolation of the active principles have made possible the administration of potent substances. The part played by deficiency of these substances in ill-health is being elucidated, but, except for distressing conditions associated with the menopause and certain disorders of menstruation and of pregnancy which are amenable to treatment by oestrogens, it is not yet clear what clinical conditions are due to simple deficiencies of sex hormones nor what effects administration of these substances have on functions other than those it is desired to modify or restore. That these substances are potent in their influence on growth and function is certain, and to administer them to enhance sexual potency without thought of other undesirable and harmful effects is unjustifiable in the present state of knowledge.

The influences of the pituitary on sex function and other internal secretory glands is becoming gradually more clearly defined, but the various extracts of the pituitary are apparently without action when administered orally. In spite of this many preparations containing such extracts are being given to patients in the hope that health, problematically disturbed by endocrine deficiencies, may be restored in some mysterious way, and by some complicated mechanism. It is certain that discoveries of great importance to the understanding of minor conditions of ill-health and to the establishment of the mechanism of disease are being made, and that the identification and synthesis of potent

chemical substances will offer therapeutic advances of great value, but, because of their potency and of the importance of these endocrine functions in influencing human lives, the medical profession should be especially cautious in applying these discoveries in practice.

In the treatment of diabetes mellitus the introduction of the insoluble preparations of insulin has effected an improvement, for they are absorbed more slowly, their action is spread over a longer period, and fewer injections are required. Such replacement by injection cannot imitate the natural secretion of insulin which is regulated by the level of the sugar in the blood, and if large doses are used the dangers of hypoglycaemia are greater than with soluble insulin. Zinc protamine insulin has established itself as the most useful of these compounds, as suitable by itself in selected cases, and as effecting a more efficient form of replacement when used in combination with soluble insulin (see also p. 69).

Vitamin therapy

It has already been pointed out that the increasing knowledge of dietetic requirements indicates how faulty growth and minor degrees of ill-health may be prevented by an adequate dietary, and that it has not recently been possible to assign any disease of hitherto unknown aetiology to the list of deficiency diseases. The advances in curative therapy in this field depend on the isolation of active principles, particularly the components of the vitamin B complex. Thus pellagra is found to be due to lack of nicotinic acid, and to be cured by administering this substance, and the neuritis and cardiac lesions of beri-beri to be cured by administering aneurin. The isolation of these active principles and their therapeutic effects have made it possible to analyse the symptoms in patients, and it is becoming clear that pure deficiencies are exceptional and that, although in any individual case a deficiency of one of these principles dominates the symptomatology, deficiencies of other principles also are usually present. Aneurin is efficacious in the polyneuritis associated with chronic alcoholism, and its trial in other forms of neuritis constitutes at present an experiment to determine aetiology, for success in treatment can be regarded as indicative of a deficiency of this vitamin, and possibly of other active principles associated with it.

The experiments with vitamins K and P are not yet sufficiently advanced for their significance to be assessed, but it appears that knowledge of conditions associated with bleeding and difficulties in haemostasis will be increased by these studies, and will be followed by improved methods of treatment.

The discovery that calciferol is not the active principle present in the natural sources of vitamin D such as the fish-liver oils, and that this active principle, irradiated 7-dehydrocholesterol, at present called vitamin D₃, is curative in certain conditions in animals when calciferol fails, has not necessitated any change in the preparations used in therapeutics, for the observations so far reported indicate that human rickets and other conditions associated with disturbed calcium metabolism in patients respond similarly to calciferol and to vitamin D₃.

Radiotherapy

In spite of the great advances by physicists in the knowledge of the properties of electricity and other forms of wave motion, the application to therapeutics of radiology advances slowly. Improvements in details of technique are giving better results in neoplastic and inflammatory diseases, and, although cures are effected more frequently in isolated cases and the conditions in which such success can be expected are being more clearly defined, treatment by X-rays and by radium is still largely palliative. It would, however, seem that such sources of enormous power must soon be utilized more successfully in the cure of disease.

THE MECHANISM OF SYMPTOMS AND SYMPTOMATIC TREATMENT

Efficient treatment depends on a clear visualization of the processes that are disturbing health and the significance of the body's reactions to them. The treatment and management of each individual depend on such visualization, and the conditions vary from individual to individual, and are recognized by a study of his symptoms. Advances in knowledge of the mechanism and significance of symptoms are therefore of great importance, for in the absence of knowledge of a cause, and so of curative treatment, the therapy and management of a patient must be based on symptoms.

Pain and insomnia

Of all symptoms pain is probably the most common, and is important not only for its diagnostic value, but also because of its interference with the physical and mental rest that is so essential for defence and recovery. The recent investigations of Lewis and of Kellgren on the anatomy of pain fibres and on the segmental distribution of pain due to experimental lesions of deep somatic structures are notable advances. The production of pain by chemical substances of intrinsic origin and associated with ischaemia demonstrated by Lewis some years ago has not been challenged, and has gained acceptance as the explanation of the pain associated with intermittent claudication and with various forms of cardiac disease. The cause and pathways of visceral pain are still the subjects of controversy, but Kellgren's work holds out promise that the significance of abdominal pains which are such important symptoms of lesions of the abdominal viscera may soon be clarified.

Pain and insomnia may powerfully interfere with rest and recovery, and, though morphine satisfies the immediate requirements, the dangers of disastrous habit-formation and addiction have led to the search for synthetic modifications free from these drawbacks. So far this search has not been successful, and, if the new compounds have some advantages, these are of little importance because the dangers of addiction have not been eliminated.

New hypnotics of the barbitone group continue to appear, but none of them has so far been accepted as an improvement on barbitone and phenobarbitone and their soluble sodium derivatives. The products of this type that act quickly and for a short time, such as sodium evipan and sodium amytal, are valuable as basal anaesthetics and as anaesthetics for intravenous administration. In the treatment of epilepsy also new substances of this type have been introduced, but so far there is no convincing evidence that they will replace phenobarbitone and potassium bromide.

Vascular hypertension

Another symptom that is attracting much attention at present and of which valuable knowledge is accumulating is vascular hypertension. The experiments of Goldblatt showed that a rise of systemic blood-pressure results from occlusion of the renal arteries, and there is evidence in favour both of a neurogenic and of a chemical mechanism responsible for this reaction. The problems of the relationship of renal and arterial disease to hypertension, and of the significance of essential hypertension, may be solved as the result of these investigations, but at least a better understanding of a common reaction and a symptom associated with much ill-health will result.

No effective drug treatment for hypertension has yet been discovered, and attention is being directed to surgical methods, such as sympathectomy, coeliac ganglionectomy, and adrenalectomy. Such procedures may lower the blood pressure temporarily and sometimes succeed in relieving symptoms permanently, but complete success cannot be expected until the pathology of

essential hypertension is elucidated. In hypertension associated with the menopause the administration of oestrogen seems to be without effect on the blood pressure, although relief from other vasomotor symptoms is produced so long as this substance continues to be given. In spite of improved knowledge of the involuntary nervous system and of chemical transmitters the treatment of the vasospastic conditions continues to be unsatisfactory. In vasospastic conditions of the retinal arteries success following the local subconjunctival injection of acetylcholine continues to be reported, and in the treatment of migraine ergotamine tartrate remains the only measure of promise, though its value is limited. For the vascular diseases of the lower limbs with intermittent claudication several new remedies have been introduced, and, although favourable reports on the effects of eupaverin and others have appeared, there does not seem to be any advance on the empirical treatment by the injection of hypertonic saline solution.

Heart disease

In the study of the symptoms and signs of heart disease and of heart failure the lesions and functions of the heart muscle monopolize attention. In this connexion the development of chest leads has expanded the value of the electrocardiograph, and much evidence is being collected enabling a more accurate estimate to be made of the damage to, and the reaction of, the separate chambers, and of the pericardium. The examination of the heart with the fluoroscopic screen is a parallel method of study and adds additional and complementary knowledge. Methods for determining the minute volume of the circulation and the total volume of the circulating blood are improving but are yet scarcely standardized or sufficiently simplified for general use in clinical studies. Venous pressures and pulmonary circulation rates can, however, readily be determined and are proving of value in the understanding of the ways in which the distribution of blood and the gradients of pressure are altered by disease. That heart failure may arise in various ways is becoming appreciated, and the underlying factors associated with greater stresses on both the left and right ventricle recognized. The features of pulmonary embolism and its early diagnosis are becoming clearer, and this may lead to the prevention and treatment of an accident that is important for its consequences and for the uncertainty it imparts to the chances of success in certain types of surgical operation.

Much thought and investigation are being directed to the control of blood flow through the coronary arteries in view of its importance to myocardial ischaemia and infarction, angina pectoris, and acute heart failure. Irreversible disease of the arteries is commonly present so that the attempts to reinforce the blood supply to the myocardium by surgical measures such as cardio-omentopexy are logical. Results are encouraging and, as improvements in the details of the methods and technique develop, this may well prove to be a valuable and efficient treatment. The only drug that seems to be effective, other than for immediate relief in attacks of angina of effort, is theophylline with ethylenediamine (euphyllin) which has a slight dilator action on the coronary arteries. Its success therefore depends on the degree to which the diseased and sclerosed arteries can be dilated to increase the blood supply to the ventricular muscle.

Digitalis and its allies still hold the principal place in the treatment of heart failure, but the mercurial diuretics, such as mersalyl (salyrgan), are receiving increasing recognition as adjuvants even in the absence of obvious oedema, and the more practical methods of administering oxygen by nasal tubes and nasal masks have extended the use of this means of affording relief.

Haematology

Such rapid and startling advances in haematology occurred a few years ago that a period of consolidation and of slower progress may be expected. The examination of bone marrow by sternal puncture adds important information to that obtained by the examination of the peripheral blood and is becoming a simple clinical procedure. Standardization of the methods for the quantification of the various cells and of nomenclature will add to the value of sternal puncture, but it has already provided much knowledge of the stages in blood formation at which disturbances occur. The rarer and atypical forms of anaemia are being studied and brought into line, and general principles of pathology are evolving. The clotting of blood and its relation to the varieties of bleeding diseases is attracting renewed attention and should lead to progress in knowledge of the plasma proteins and their alteration in disease. The importance of the formed elements of the blood in the maintenance of health and the resistance to disease has long been recognized, and the newer knowledge of these is extending to the tissues in which they originate, and to the reticulo-endothelial system.

Tests of renal and hepatic functions

The search for more satisfactory tests of renal and hepatic functions continues without striking results, so that the ability to gauge accurately the degree of impairment of the function of the liver and the kidneys and to aid these organs has not improved.

Blood-levels of various constituents

The renewed study of blood-sugar levels in arterial and venous bloods promises a greater accuracy in assessing disorders in carbohydrate metabolism and in their correction.

Much work is being done on the blood-levels of sodium, potassium and chlorides, and on the estimation of blood volumes, and this should prove helpful in two directions. The function of the adrenal cortex is associated with the levels in the blood, and the excretion, of sodium, potassium, and chlorides, and may prove to be affected in conditions other than Addison's disease. The introduction of potent cortical extracts and active principles makes it possible to correct deficiencies in cortical function. Following haematemesis, and in other conditions associated with loss of fluids and dehydration, accurate studies of total circulatory fluid and of blood chemistry are likely to give clearer indications for treatment in such conditions in which at present the degree of dehydration is frequently not recognized, and, if recognized, is usually treated by the administration of blood or of physiological saline. The indications for administering glucose solutions or hypertonic saline instead of physiological saline will certainly become clearer in the near future, and offer important advances in the treatment of haematemesis and in the pre- and post-operative management of patients.

Gastric disorders

Disorders of digestion and symptoms of dyspepsia are present in a large proportion of the patients who seek help and advice and, since the introduction of examination by the opaque meal, advances have been slow. The use of the gastroscope is becoming more wide-spread, and its value in the early diagnosis of gastric carcinoma seems assured, but its principal achievement has been the recognition of gastritis which is frequently present in conditions in which it was not previously suspected. The relation of symptoms of dyspepsia to pathological states of the gastric mucosa should shortly be ascertained, and the early stages in the development of peptic ulcer and of carcinoma may be determined.

Disorders of the movements and the functions of the muscles of the gastrointestinal tract are probably more important in determining symptoms than are disorders of secretion or the presence of inflammations of the mucous membranes, and these are largely controlled by the involuntary nervous system. Increased knowledge of the anatomy and physiology of this system and of the lesions that can result from its abnormal functioning should be fruitful. The connexions of this system with centres in the hypothalamus and its intimate relation with chemical substances for the transmission of its effects are being elucidated, and these lines of study should result in greater accuracy in diagnosis and appreciation of the significance of symptoms in disturbance of abdominal viscera.

The dangers of alkalosis in the treatment of peptic ulcer have stimulated the trials of antacids, such as aluminium silicate (kaolin), but their advantages have not yet been generally recognized, and the need for alkalization of the stomach contents to promote the healing of peptic ulcer has been questioned, the use of alkalis being regarded as merely a treatment for the relief of pain.

Disorders of the colon

Disorders of the colon always attract attention because of their high incidence, and, although no new principles in treatment have developed, there is need for continued emphasis on the dangers of purgation, the advantages of habit formation, the use of substances to increase the bulk and soften the consistency of the contents of the colon, and of physical aids to evacuation. Spastic conditions and loss of normal reflexes from continued inhibition are recognized as much more common than atony of the colon.

Psychotherapy

Perhaps the most striking change that is taking place in symptomatic treatment is due to the acknowledgement by medical men of the preponderance of psychological causes of symptoms, and the recognition by the public of this factor in their production. There is therefore less demand on the part of patients for treatment by drugs, and a greater acquiescence in treatment by explanation and reassurance, and by adjustments in their habits and environmental and social relationships.

As the science of dietetics expands, advice can be given with confidence that will obviate resort to fashionable fads and exploitations that are not without dangers; and, as the value of general fitness in the prevention of ill-health obtains wider recognition, treatment by physical exercises and general hygienic measures are taking the place of drugs and other substances of doubtful value and even potential harm.

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GENERAL SURGERY

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Although there have been no spectacular advances in surgery during the past ten years, nevertheless innumerable improvements and refinements have been made in all its branches, maintaining for the most part a steady onward progress.

Disease, in whichever part of the body it may be present, is often open to a direct and frequently successful attack by the surgeon. Areas such as the brain and heart, formerly dangerous to expose, are now within the province of any trained operator who has learned how to prevent or combat surgical shock and infection of his wounds, but such efforts will not be successful unless dictated by accurate diagnosis.

The development of positive pressure and intratracheal methods of anaesthesia have made exploration of the lung relatively safe, and removal of a diseased lobe is a frequent undertaking. But, though general principles underlie successful operative interference in all fields, the process of rationalization has occurred in surgery simultaneously with that of the business world, and there is a tendency to a very high degree of specialization. This is exemplified in neurosurgery and genito-urinary surgery, in which the specialist confines himself to the study and practice of one particular system of the body, and understands thoroughly not merely the surgical pathology and the necessities of special surgical attack, but also the use of all ancillary aids to diagnosis and their interpretation, and the special after-treatment that may be required. But, though the day of the general surgeon who was equal to the best in any and all branches of surgery has drawn to a close, the best specialist must have had a thorough grounding in general surgery before devoting himself to the study of his own particular field.

The technical side of surgery is now so nearly standardized that it can be acquired in a comparatively short time. This in itself carries grave disadvantages, as operative ability is often far in advance of sound surgical knowledge and judgement, which can be gained only by constant experience ripened by visits to other surgical clinics in this country and abroad and the study of world literature. Further progress in surgery will depend on the more accurate diagnosis of the nature and extent of disease, careful study of the individual patient, and more skilled pre-operative and post-operative care. The 'look and see' policy of yesterday has been replaced by a carefully planned operation on a patient, the limits of whose disease have been meticulously mapped out and whose stamina and 'operation worthiness' have been exactly determined.

DIAGNOSIS

Diagnosis still depends mainly on the scrutiny of a painstaking history and a thorough clinical examination, but other aids have been developed to a remarkable extent and yield very precise information.

Radiology

The science of radiology has steadily advanced and now occupies an important place in everyday surgery. Skiagrams are photographs of shadows and

outlines either plain or rendered clear by radio-opaque fluids, solids, or gases, but motor function of hollow viscera, e.g. the gastro-intestinal tract or the renal pelvis, may be observed under the fluorescent screen. It must be realized that the findings of these dynamic observations are often more useful and important than the study of the static films. Radiology also aids in the estimation of function of certain secretory viscera such as the kidney and the gall-bladder.

Endoscopy

Various optical systems incorporated with instruments for their introduction enable us to obtain precise information of the interior of most of the tubes and cavities of the body. The cystoscope is perhaps the most accurate of these, but the sigmoidoscope, the bronchoscope, the oesophagoscope, and the thoracoscope have all their value. The latest addition to this armamentarium is the gastroscope, which allows direct inspection of the gastric mucosa. There is also a revival of the method of laparoscopy, but as yet it has not established its proper level.

Biochemical tests

The biochemist also gives invaluable aid in the solution of diagnostic problems. His chief office lies in his ability to determine by special tests the functional capacity of viscera, such as the kidney, the pancreas, the stomach, and to a much lesser degree the liver, thus enabling the surgeon not only to estimate the relative risk of an operation on each particular patient, but also to diminish that risk by taking the appropriate pre-operative precautions.

The psychical effect of disease on various mental types is ill-understood, and as yet the psychologist has had little opportunity to add his share in steering the patient through illness to health.

Pre-operative preparation demands co-operation among physicians, surgeons, and clinical pathologists, and it is perhaps this co-operation that is the striking feature of present-day surgery.

DIETETICS

The science of nutrition and the practice of dietetics has so far not been fully utilized in surgery, but in future it must take a larger share in pre-operative preparation. Many hospital patients suffer from defective nutrition which may take the form of sub-scurvy, and this must be corrected by adequate diet before operation is undertaken. The low-protein diet adopted in cases of hepatic insufficiency, and the addition of vitamin preparations, such as ascorbic acid and vitamin K, to the diets of jaundiced patients, are recent tendencies.

Certain pre-operative and post-operative diets have been examined and found deficient in mineral salts, vitamins, and even water, and some gastrostomy diets have not had a sufficiently high calorific value. A dehydrated patient is a bad surgical risk, and wherever possible operation should be postponed until the circulating fluid volume has been restored to normal by the administration of liquids by mouth, bowel, or subcutaneously or intravenously.

If a patient is suffering from anaemia this should be remedied by the usual medical measures or by blood transfusion, and the response to these plans may be a useful index of the recuperative power. The continuous blood drip is an invaluable method of restoring blood volume and value when operations on bleeding patients are necessary.

ANAESTHESIA

A number of elderly men suffer from latent uraemia due perhaps to a symptomless urinary tract obstruction, and a general anaesthetic may be sufficient to cause death, irrespective of the operation. Routine examination may disclose entirely unsuspected renal insufficiency, which should be treated before the condition causing the patient's symptoms is dealt with.

Choice of methods

The condition of the patient influences the anaesthetist in his choice of method, and in all difficult cases this should be decided in collaboration with the surgeon who is responsible for the outcome of the case. Many new anaesthetic drugs have been introduced, but the search for the perfect anaesthetic still continues. At present gas and oxygen anaesthesia is largely used as a routine, but cyclopropane is on trial. Spinal anaesthesia is especially valuable when abdominal relaxation is necessary, and to prevent shock, and it has the advantage of producing the minimal degree of upset of liver function. But there is a tendency for anaesthetic apparatus to become too complicated and cumbersome, and it ought not to be forgotten that the great operative triumphs of the immediate past were carried out under very simple and direct methods of anaesthesia.

Local anaesthesia

Local anaesthesia for major surgery has not been largely used in this country, but in certain cases it is invaluable, and all young surgeons should be thoroughly trained in its application, if for no other reason than to acquire the saving grace of gentleness in operative manipulation.

Intravenous anaesthesia

The intravenous anaesthetics are useful for short operations or as a pleasant method of induction of anaesthesia, and are very useful in neurosurgery, but they should never be employed in conditions of toxæmia.

TYPES OF OPERATION

The ultimate responsibility for the patient's safe return to permanent health remains with the surgeon, and he must decide the type of operation best suited to each particular case. Though operative technique is now fairly well standardized, there are a bewildering number of methods available for every condition. New operations are described and become fashionable for a time, and some of them prove useful, but the real test is in the after-results.

It is essential for the surgeon to be familiar with all techniques in his speciality, but he must be the slave of none, and well-balanced judgement is more important than mere operative dexterity.

ANTISEPTICS

In everyday surgery, aseptic methods are the rule, antiseptics being used much more sparingly than in the past. Nevertheless, infection of wounds still occurs, and though usually mild may result in delayed healing and convalescence and slight rises of temperature with resulting scars that are not perfect. Such mild unobtrusive infections may have a relationship to thrombosis and pulmonary embolism.

DRUGS

New drugs, particularly the sulphanilamide group, have been found useful in combating infection, but when a wound goes wrong the surgeon should

endeavour to trace the cause, which may be an error in technique or the consequence of a carrier in the field of operation.

SUTURES AND LIGATURES

Sutures of living tissue such as fascia are used in certain cases and appear to be a definite advance in the repair of some types of hernia. They introduce a new principle, for they not only approximate and lace parts together, but become incorporated with the tissue and survive as permanent fibrous strands.

There is a tendency to return to the use of silk or linen thread for sutures and ligatures, but, as these materials cannot be depended upon to disappear by absorption, they every now and again form a nidus of irritation and cause sinuses. They are not ideal in surgery, and their use cannot be defended.

DIATHERMY

During the last few years the electric knife has been on trial, but it has not displaced the ordinary scalpel. It was claimed that it caused less traumatism, diminished haemorrhage by sealing small vessels as they were divided, and warmed the patient instead of causing chill, so that shock was prevented. Though these claims can probably be justified, it has never come into general use, but it is admittedly invaluable in dealing with tumours of the nervous system, and for that purpose its use seems firmly established.

NECESSITY FOR PHYSIOLOGICAL KNOWLEDGE

The training of the surgeon has altered somewhat; instead of concentrating on anatomy and pathology, he must now also have a thorough understanding of physiological processes. This is best exemplified in the surgery of the sympathetic nervous system and ductless glands. Indeed, surgeons have been able to make valuable contributions to physiological knowledge and the surgery of the ductless glands has made great strides since the day of George Murray. Generalized bone disease, *ostertis fibrosa cystica*, is apparently due to hypertrophy or adenomatous development of the parathyroids, and is often favourably influenced by their excision. Adrenal tumours have been diagnosed as the cause of virilism, and removal has restored to the patient the natural attributes of her sex.

It is probable that increasing knowledge will lead to greater surgical interference with the hormone-producing glands, and replacement, or even substitution surgery by transplants and grafts, will be used in spite of the great enterprise of the manufacturing chemists in the synthesizing of these products. It is difficult to foresee to what extent this form of therapy will be carried.

Crite has offered new concepts of disease in the problem of essential hypertension and has elaborated operations of sympathectomy and partial adrenalectomy for its relief. This and other operations with the same end in view are being increasingly practised at present and with a modicum of encouraging results.

SURGERY OF SPECIAL ORGANS

Thoracic operations

The old special dangers of operations on the thorax have been eliminated, and this has given an impetus to all types of surgical adventures. An experienced operator with adequate training is able without undue risk to the patient to remove a lobe or even a whole lung. A portion of muscle or omentum can be grafted on to the heart to produce an additional blood supply. The value of these operations, has, however, depended on the appropriate indications, and they can only assist and not supplant Nature's curative efforts. Some years

of experience and careful follow-up are necessary before the true final results can be assessed. A careful balance should be kept between what unaided Nature can accomplish and the possible damage by curative surgery. It is a mistake to be in a hurry to endeavour to short-circuit natural cure.

Genito-urinary system

In the genito-urinary system conservatism is the modern tendency; for example, preservation of the organ whenever possible, plastic operations for hydronephrosis, and removal of stones only, with subsequent sterilization of the urine by means of urinary antiseptics.

Transurethral resections for prostatic disease are popular, but the first enthusiasm for this type of operation in all cases has been somewhat dampened by careful study of after-results, and it is recognized that some enlarged prostates, possibly 20 per cent, are best treated by suprapubic enucleation. The technique of ureter transplantation is now on a firm footing, and many patients have survived and maintained good health over periods of many years.

Gall-bladder surgery

The surgery of the gall-bladder has altered little, apart from the more careful pre-operative treatment of jaundiced patients, and those whose liver function is damaged. The present-day outlook can be expressed by saying that it is now the rule to pay as much regard to the patient as to the stones. Cholecystectomy is the present method of choice for the treatment of gall-stones limited to the gall-bladder. Nevertheless, many papers have been published giving after-histories of cholecystectomized patients, many of whom have not been entirely relieved of their symptoms, or who have acquired new troubles. It may be that in some cases there are good grounds for a reversion to the old method of drainage with preservation of the gall-bladder, especially as there is just a possibility that the viscus may be responsible for a hormone which serves a useful function in the preservation of the hepato-pancreatic and gastro-duodenal systems.

Though not many examples of injury to the common duct during the performance of cholecystectomy have been published in this country, the accident is not infrequent and is often regrettably serious in its consequences.

Peptic ulcer

Treatment of peptic ulceration of the gastro-intestinal tract is in the first place left almost entirely to the physicians, who call in their surgical colleagues when they consider it necessary. The modern fashion is to perform radical operations, such as extensive gastrectomies, hoping thereby to prevent the complications of recurrent ulceration. But it is absurd to discard a well-tried operation such as gastro-enterostomy which has excellent results to its credit, especially when ulceration is combined with obstruction. It must be recognized that at best the extensive resections are often only palliatives and may bring new diseases, such as anaemia, in their train, but until we know how to combat the pernicious ulcer tendency we must continue to employ them with discretion.

TRAUMATIC SURGERY

In traumatic surgery the battle between restoration of function and anatomical alignment has been settled by fusion, for careful reduction of the fracture and fixation by plaster of Paris allows of early restoration of function in many cases. Internal splints have been largely discarded, at times perhaps to the patients' detriment, and reliance placed entirely on external fixation. Fracture results have been much improved by the greater interest and closer attention which can be given in fracture clinics and rehabilitation centres.

TREATMENT OF CANCER

Surgical extirpation

There have been no major advances in the treatment of cancer, in spite of the vast amount of research work in this subject. In the great majority of cases the best possible treatment still remains early and thorough removal of the growth, together with a wide area of healthy tissue, and the path of probable malignant invasion as represented by the corresponding lymphatic glands, together with the intervening lymph channels. Unfortunately this is not always possible, and the surgeon must then be content to remove the growth and glands in stages.

Irradiation

Radium and X-ray therapy have not yet fulfilled the high hopes entertained for them some years ago. It is of course recognized that some growths are favourably affected by radiotherapy, and that in some few situations the latter is perhaps the method of choice. In other cases growths prove radio-resistant, and, even when treated by experts, they do not respond, and there is a justifiable suspicion that sometimes irradiation encourages dissemination.

In spite of its disadvantages, however, the surgeon must always be grateful that irradiation is available for the treatment of certain types of cancer. Irradiation is most useful in situations where the mortality of radical operations is too high, or where the mutilation involved is too great, or the after-results discouraging. It is also valuable as a palliative measure when the growth is beyond the limits of surgery.

Combined treatment

Combined methods of treatment, namely irradiation of the primary growth with excision of the lymphatic fields, are in vogue. Another tendency has been to be content with local excision of the growth and reliance on irradiation to destroy remaining cells, but this plan should be deprecated. Quite clearly there is no justification for the haphazard use of irradiation, and it must only be used after most careful consideration of the individual problem. In trying to assess the relative values of the methods of treatment available, only the work of those properly trained in either field can be compared.

More radical excision

Confronted with the disappointments of irradiation many surgeons are extending the scope of radical excisions. Malignant disease of the bladder is an example, and in many cases excision of the whole viscus with transplantation of the ureters into the bowel has yielded encouraging results. Carcinoma of the oesophagus is still claiming much attention, and quite recently several cases have been recorded in which the neoplasm has been successfully excised, but only the ultimate results can determine the real value of the operation.

But the search must still go on for some remedy that will fulfil the dictum laid down by John Hunter many years ago to the effect that a real cure would be some method that would 'so alter the constitution of the parts that the cancer would disappear'. To this end many plans have recently been tried, such as short-wave diathermy, artificial pyrexia, and the use of sera, but all have so far been without success.

There is, however, less ground than ever for discouragement, for early operation based on pathological study and conscientiously carried out continues to keep many patients alive and well after the ten-year period.

OBSTETRICS AND GYNAECOLOGY

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OBSTETRICS

Maternal nutrition

Much useful work has been carried out within recent years on the *optimal diet for pregnancy*. It is generally agreed that, so long as a woman receives a good average standard diet, there is no need for supplementary additions, and in the present state of our knowledge there is no doubt that natural sources are to be preferred to artificial and synthetic supplies.

Mellanby laid it down that an adequate diet for pregnancy and lactation should contain 2 pints of milk daily, 1 or 2 substantial servings of green vegetables (cabbage, spinach, or lettuce), 1 or 2 eggs, 1 apple, an orange or some fresh fruit, sea-fish twice or more times a week, calf's liver once a week, and that the rest of the diet may be made up according to the woman's tastes. Such a diet is of course relatively expensive, and there is no doubt that, for large numbers of pregnant women, it is prohibitive, with the result that gross deficiency in essential elements is very common. Especially in the poor, though by no means confined to them, relative deficiency in the mineral elements (calcium, phosphorus, iron, and iodine) and in the vitamins, A, C, and D is a commonplace.

A great deal is being done by State and Municipal effort to supplement the diet of the necessitous woman but, despite this, it is the opinion of those best able to judge that gross deficiency exists, and that it is responsible for much maternal morbidity, and possibly also for much faulty foetal development and deficiency in the milk of the nursing mother.

Kirsten Uthmeim-Toverud makes a further contribution to the valuable work which she has already published on the influence of maternal nutrition on mother and child. In a selected area in Norway the women were carefully supervised throughout pregnancy, and the influence of this supervision on the welfare of the infants after birth was traced. At the beginning 32 per cent of the women were found to be anaemic, 31 per cent to be suffering from deficiency in vitamin A, 39 per cent to have a low blood-calcium level, and 49 per cent a low ascorbic acid level. Further, vitamin A deficiency was found in 36 per cent of the lactating women. The pregnant and lactating women under treatment developed normal values. Amongst the effects of the improvement in the dietetic and general control there was a distinct lowering in the premature-birth rate (from 8 to 2 per cent). The influence of diet in lowering the premature-birth rate has been referred to by Toverud in previous records. There was, further, a lowering in the incidence of infantile rickets from 19.7 per cent, in the children of mothers whose pregnancy was not controlled, to 3.8 per cent, in those of mothers with a controlled pregnancy, and a lowering of the incidence of caries in the same groups from 82 to 30 per cent.

Another recent article of value along similar lines is that of Finola, Trump,

and Grimson, who treated 33 pregnant women with dicalcium phosphate and viosterol (calciferol), 25 serving as controls. On X-ray examination of the infants after birth it was found that the skull, the ribs, and the epiphyses at the knee were denser in the treated than in the untreated cases.

Such observations have considerable scientific interest in demonstrating the influence of maternal nutrition on vital processes in the child's development. At the same time they do not in themselves justify the indiscriminate use of supplements of minerals and vitamins in the antenatal woman, because, as the authors wisely remark, an increased condensation of the foetal head may, by rendering birth difficult, be harmful. One of the great drawbacks facing maternal hygiene is that, when it is impossible or inexpedient to ration the mother with a full and abundant natural diet, we are still so ignorant of the optimal requirements of some of the essential and protective foods that artificial administration, unless wisely directed, may do more harm than good.

Habitual abortion

The value of vitamin E in cases of habitual abortion is constantly receiving fresh confirmation. Much of the divergent opinion in regard to its value would seem undoubtedly to arise from the well-known fact that wheat-germ oil, the most common form in which it is administered, rapidly loses its activity. Evan Shute states that it retains its potency for about eight weeks only. For this reason many obstetricians rely rather on the employment of progesterone (one international unit thrice weekly) or prolan (100 rat units thrice weekly), which, however, should not be continued beyond the 36th week of pregnancy. The published records indicate that these methods give a successful result in anything from 70 to 90 per cent of cases.

It has been suggested, though on this matter the scientific evidence is not yet complete, that the identity of the results obtained with the above three procedures arises from the fact that vitamin E is concerned with the physiological maintenance of the prolan-progesterone mechanism of pregnancy.

Toxaemia

Browne and G. H. Dodds have published recently a very extensive analysis of the subsequent progress in 400 patients suffering from the toxaemia of late pregnancy. These women had a total of 589 pregnancies, and they were followed up for periods varying from 12 years to 6 months. The cases were grouped into pre-eclamptic toxaemia, eclampsia, hypertension, chronic nephritis, and recurrent toxaemia. Both in pre-eclampsia and in eclampsia these authors found the follow-up to show that the residual lesion was invariably hypertension (50.9 and 60.8 per cent respectively), and that, contrary to the opinion expressed by other workers, chronic nephritis never developed. The older the patient, the greater was her parity, and the higher the blood pressure during the pregnancy and the longer the duration of the illness, the greater seemed the liability to the ultimate occurrence of residual hypertension. They found that, of the hypertensive patients, 9.2 per cent had died during the 12-year period. They satisfied themselves, however, that the majority of patients with simple hypertension passed through pregnancy without any demonstrable deterioration in their general condition. In most cases of recurrent toxaemia the patient had hypertension during the interval between the pregnancies, and they considered that the remainder were 'potential hypertensives' and that in all there was a familial hypertensive tendency. This, they believe, suggests that patients who develop residual hypertension after pre-eclamptic toxaemia and eclampsia have a familial tendency to the disease, which pregnancy has merely revealed and the onset of which pregnancy has hastened, so that it occurs at an earlier period than it would otherwise have done.

Browne and Dodds found chronic nephritis complicating pregnancy to be

rare; it occurred in only 17 out of their series of 400 patients. The ultimate prognosis is usually bad, and 29·4 per cent of their patients died in the 12-year period. Pregnancy was always a serious risk to such patients, but, paradoxically, in 50 per cent of the cases the patient did not seem to be any worse as a result of it.

Kellar agrees with Browne and Dodds in finding that the pathological records of women dying months or years after a toxic pregnancy indicate that, in the majority, the death occurred from the effects of prolonged hypertension. He further agrees in stating that potential or incipient essential hypertension is a predisposing cause of toxæmia and its recurrence.

Foetal respiration

Within recent years increased interest has been shown in the question of whether the foetus exhibits true respiratory movements before birth. Bonar *et al.* have carried out a careful series of observations, and claim to have shown that the foetus *in utero* breathes, with the production of a tidal flow of amniotic fluid backwards and forwards in the lungs. There is also much corroborative evidence from lower animals.

It is known that after birth a still-born child may have large quantities of epidermal material in the lung alveoli, inhaled with the liquor amnii. It has usually been supposed that this was ascribable merely to the premature inspiratory efforts of an asphyxiated and dying child, but this interpretation would not now seem to be always adequate. It is probable also that the well-authenticated instances of congenital broncho-pneumonia in the infant can be explained by the above mechanism.

Uterine inertia

Jeffcoate believes that it is more accurate to speak of 'inertia of the first stage' and 'inertia of the second stage' than of primary and secondary inertia. He claims to show that, in over 50 per cent of cases, inertia is relieved by the use of oestrogenic hormones, and that in a successful case there is usually a marked improvement in the regularity and co-ordination of the uterine action. The writer has seen successful results following the use of 50,000 to 100,000 international benzoate units, repeated if necessary after four hours.

Puerperal sepsis

One of the most outstanding facts in modern obstetric practice is the striking decline in the death-rate from puerperal sepsis. The rate in England and Wales in 1937 was the lowest during a period of twenty-seven years, that is, since the present classification was adopted. There has been a drop from 1·95 per total 1,000 births in 1934 to 0·94 in 1937. It is difficult to account adequately for this remarkable improvement. It is no doubt partly to be correlated with the drop in the death-rate in the general community from septic conditions, which has occurred over the same interval, and it is due partly to the success attendant on the introduction of the sulphonamide preparations. That it is not due exclusively to this latter factor, as has been sometimes claimed, is suggested by the fact that a similar decline occurred in communities before sulphanilamide was employed to any appreciable extent. Thus Daily has shown that, whereas between 1930 and 1936 the average annual percentage decrease in puerperal sepsis in the United States was 1·6, the percentage decrease from 1936 to 1937 was 21·4. This occurred before the sulphonamide preparations were in general use. At the same time there can be no doubt about the outstanding value of the sulphonamide group of drugs in the treatment of puerperal sepsis due to the haemolytic streptococcus. For the five-year period up to 1936 the average death-rate from puerperal sepsis from this cause in the Queen Charlotte's Hospital Isolation Block was 22·8 per cent, whereas

following the use of prontosil the average mortality during 1936-38 was 5.7 per cent.

It is becoming apparent that the wide-scale employment of these drugs is associated with a risk, the measure of which is not always appreciated. It is imperative that, when they are employed, this risk should always be remembered, and that the administrator should never embark on their use until he has familiarized himself with the symptoms indicating a toxic reaction. Colebrook states that an incomplete survey of the literature shows that there have been 35 reported deaths following the use of these drugs. He further states that, from reports reaching him privately, there is evidence that a larger number of deaths have not been reported, and with this view the writer is in agreement. Colebrook indicates also that there is reason to believe that there are unrecognized fatalities occurring, because control leucocyte-counts are not being carried out. If white-cell counts are not made at short intervals, the patient's rising fever and deteriorating general condition may readily be ascribed to an exacerbation of the septic infection for which treatment is being carried out.

It is clear that agranulocytosis resulting from the sulphonamide group of drugs is a very fatal complication, more than 50 per cent of the patients so affected having died. The condition may be met with after the use of any sulphonamide drug. Most of the cases recorded have occurred in association with sulphanilamide itself, but already 6 cases have been recorded after the use of M & B 693, as well as 3 cases of neutropenia. Colebrook states that he knows of only one death after the use of prontosil rubrum.

The relationship between the amount of the drug and the development of agranulocytosis is striking. In 24 cases reported in sufficient detail the average dose administered was 48 g., and the duration of treatment was 24 days. In only 2 cases was the total amount less than 30 g. (20 g. of M & B 693 in one case; 18 g. of sulphanilamide in the other). In no less than 11 cases out of 19, in which the details of treatment are given, the fall in the leucocyte-count took place during a second, third, or fourth course of treatment.

These data (according to Colebrook) seem to point to a fundamentally important conclusion, namely, that there is not much margin between the amount of sulphanilamide which appears to be necessary to control a severe streptococcal infection (20 to 30 g.) and that which, in some people, involves a serious risk of agranulocytosis (30 to 60 g.). It would seem therefore that there is a risk of continuing the treatment too long, in cases in which a prompt response is not obtained.

At Queen Charlotte's Hospital it has been found that, if a patient's temperature-chart and general condition do not show unmistakable improvement within the first five or six days, it is unlikely that there will be any response from further treatment. Other puerperal infections, except some by the staphylococcus, and the urinary infections by *Bact. coli*, have almost invariably not responded, and, in Colebrook's opinion, should not be treated by these drugs.

Colebrook suggests the following practical rule: If the fever subsides satisfactorily under treatment, and the general condition shows corresponding improvement, there is no need to do white-cell counts for the first six days. The drug may be continued for a further 2 or 3 days without anxiety. If, on the other hand, the temperature does not show a prompt response, or if there are other disturbing symptoms, such as headache, white-cell counts should be done every second or third day from the beginning of treatment. Similarly, in every case in which more than 25 g. has been given, or treatment prolonged for more than ten days, white-cell counts should be done at short intervals.

In view of the grave risks associated with the colourless sulphonamide preparations, Kenny makes a plea for a return to the original red compounds. She has found further that all the undesirable non-fatal side-effects

are more marked with the colourless drugs, and recommends a return to *prontosil rubrum*, and to the original moderate frequently-repeated doses suggested by Colebrook and herself in 1936. She points out that the lowest death-rate from streptococcal puerperal infection at Queen Charlotte's Hospital (5.3 per cent in 1936) was obtained with red *prontosil* with an average dose for the 68 patients treated of 18 g., as against the very much larger doses of *sulphanilamide* and M & B 693 required to bring about the same effect.

Sulphanilamide in breast milk

Stewart and Pratt find that *sulphanilamide* is excreted in human breast milk in a concentration similar to that present in the maternal blood-stream, and that the baby shows no toxic effects when there is as high a level in the milk as 7 mg. per 100 c.cm.

GYNAECOLOGY

Pulmonary embolism

Fletcher Shaw and Rickards report the death-rate from embolism in two hospitals in which the gynaecological wards were under the control of the same surgeon, and in each of which the same pre-operative and post-operative care was observed, except that in one graduated exercises after operation were employed. After 1,635 consecutive operations in the hospital, in which graduated exercises were employed, there was an incidence of fatal pulmonary embolism of 0.06 per cent, whereas after 3,618 operations in the other hospital the incidence of fatal pulmonary embolism was 0.304 per cent, that is, five times as great.

Chronic cervicitis

This subject provides a perennial source of new literature, and, following the investigation of Cruickshank and Sharman, and others (see Vol. IV, p. 575), on the effect of disturbed ovarian control on the pH of the vagina, a considerable amount of work is being published on aetiology. Thus Roblee claims to have shown that the continued exposure of the vagina to an environment of pH 6.5 to 7.5 results in a proliferation of the columnar epithelium of the cervix at the expense of the stratified epithelium, and that a secondary cervicitis develops. The exposure of the vagina, on the other hand, to a continued environment of a pH of 4 to 4.5, except in advanced cases of structural damage, results in a cure of cervicitis and in a readjustment of the epithelial balance. Roblee believes that, where there is a pathological condition of the cervix with an excessive proliferation of the columnar elements, the excessive alkaline secretion of the cervical glands disturbs still further the pH of the vagina and thus, by a vicious cycle, perpetuates the infective process. He believes that, especially in nulliparous women, the disturbed pH of the vagina is the main cause of infection, and holds that such cases should be treated by douches containing acid-fermentable material. In some cases this is followed by speedy relief. For cases of papillary erosion removal of the redundant material is necessary.

The consensus of opinion would now seem to be definitely against removal operations (amputation) and plastic repair operations (trachelorrhaphy) for chronic cervical disease, and in favour of conservative procedures based upon electro-surgery (cauterization, coagulation, conization). The writer has employed cauterization for many years, and has found that, even in advanced and long-standing cases in which repeated treatment may be required, it almost invariably gives successful results. The procedure consists of a full preliminary dilatation of the cervix to permit of free drainage during the healing process followed by superficial radial incisions of the cervix from the internal os downwards over the eroded surface. Three incisions behind and

three in front are usually sufficient with, in addition, free puncture of the isolated Nabothian cysts. The employment of oestrogenic preparations in women with evidence of ovarian hypofunction is of great value, and this applies especially to many cases of so-called 'virginal' erosion and to senile infections.

It is remarkable how quickly clinical improvement occurs after such treatment. Long-standing leucorrhoea, lower abdominal pain and discomfort, dyspareunia, bladder frequency, and general debility and anaemia are all relieved within a short time in a typical case.

Lower abdominal pain of cervical origin

In some instances lower abdominal and especially iliac fossa pain is peculiarly intractable in cases of the cervical syndrome, and for these Young carries out blockage of the rich sympathetic plexus (Frankenhauser) situated at the side of the cervix, for the purpose of removing the pain-afferent impulses coming from the cervix. The procedure consists in the injection of 2 c.cm. of proctocaine, an oily alcoholic preparation containing procaine, into the tissues adjacent to the isthmus of the cervix on each side. This results in immediate and complete relief of the pain in about 50 per cent of cases, and partial relief in a further 30 per cent. Unfortunately, in a proportion of cases, the relief lasts for only about 3 months, and for these further treatment is indicated. It is important that this frequent cervical source of lower abdominal and pelvic pain should be remembered, as otherwise very grave errors in diagnosis and treatment may be perpetrated. Curtis of Chicago has recently called attention to the same facts.

The irritable bladder and cervicitis

Many cases of chronic cervicitis are associated with irritability of the bladder. In many such cases there is no demonstrable pathological lesion in the urinary tract: the urine is normal, the bladder on cystoscopic examination is found to be healthy, its capacity is adequate, and the ureters and kidneys exhibit no morbid changes. According to Young and Cunningham, the bladder irritability in such women is reflex, and is dependent upon excessive sympathetic stimulation from the cervical disease. A large proportion of such patients obtain immediate relief by the injection of 1.5 to 2 c.cm. of proctocaine into the tissues adjacent to the bladder base on each side, employing a needle passed *obliquely upwards and outwards from the cervix which is pulled down, the patient being in the lithotomy position.*

Sedimentation rate in gynaecology

This procedure has firmly established itself as one of the most valuable diagnostic measures available to the gynaecologist. It is of special value in cases in which the differentiation is between an infective lesion, e.g. salpingitis, and ectopic pregnancy. In the writer's experience an *active* infective lesion in the pelvis is invariably associated with an abnormally rapid rate, whereas, with very few exceptions (in 10 years he has seen only one exception) the rate is normal in ectopic pregnancy. The value of the test in cases in which an accurate and rapid diagnosis may be of supreme importance can hardly be over-estimated. The same advantage is, however, not apparent in cases of non-pelvic infective conditions, and Lintgen and Fry found that 48 per cent of patients with acute appendicitis have a normal sedimentation rate.

ENDOCRINOLOGY

Synthetic oestrogens

E. C. Dodds (1938) and his co-workers have described a series of synthetic products with which they have been able to induce in laboratory animals the

characteristic phenomena of oestrus. One of these substances, diethylstilboestrol, is two and half times as powerful as oestrone in ovariectomized rats, and it also possesses the great advantage of being more effective than the natural oestrogens when taken by mouth.

The clinical application of this material has been carried out under the auspices of the Medical Research Council and has been the subject of a number of recent interesting and valuable papers. Kellar and Sutherland find that the drug, when given by mouth in suitable doses, gives results more or less comparable to those of the natural oestrogens. In cases with simple menopausal symptoms they recommend that treatment should commence with a dosage of 2 mg. daily by mouth, and be increased if necessary. In leucoplakia, senile vaginitis, and kraurosis treatment should commence with a minimal dosage of 5 mg. daily for a week, and then be reduced as necessary.

A disadvantage of diethylstilboestrol is its tendency to produce nausea and vomiting in some patients. This tendency is not dependent upon the dose, and in some few instances it may be so troublesome as to preclude the use of the drug. Dodds and his collaborators are investigating the possibilities of other synthetic products with the object of discovering forms without this disadvantage.

There can be no doubt that these discoveries open out the possibility of important new developments through which we may justifiably look forward to the appearance of oestrogenic preparations possessing the double advantage of being cheaper and being active by mouth.

Control of milk secretion

It has now been definitely established that, in cases in which lactation has to be arrested in the early puerperium, for example, because of foetal death, or illness of the mother, the most effective method is the administration of adequate doses of an oestrogenic preparation. Kellar and Sutherland report cases in which 3 mg. of diethylstilboestrol, administered orally three times daily, was sufficient, either before or after engorgement of the breasts had occurred. It is believed that the oestrogen acts by inhibiting the galactogogic activity of the anterior lobe of the pituitary.

Prolactin (the anterior pituitary galactotrophic hormone) has been employed successfully to increase the secretion of breast milk. There are now on the market active and reliable preparations (physolactin and prolactin) safe from the undesirable side-effects upon the gonads and sugar-metabolism of the earlier experimental products. Kenny and King have published a series of carefully controlled observations in women with deficient lactation in whom satisfactory nursing has been established by the administration of prolactin in the early and later stages of the lactation period.

Male sex-hormone in gynaecology

Within recent years a number of communications have appeared on the use of testosterone propionate in gynaecological conditions such as metropathia haemorrhagica, dysmenorrhoea, and fibromyoma, but it is still too early to pronounce definitely on the value of this agent. It would seem, however, that in appropriate dosage (total dosage of about 1,000 mg.) it is possible to arrest menstruation when this is desired, as in excessive menstrual bleeding associated with endometrial hyperplasia, and in effect to induce a temporary artificial menopause. In such cases menstruation may be arrested for a period of three or four months. As undesirable virilizing results are apt to occur, such as hirsutism and deepening of the voice, and also an acneiform eruption of the face, it is important that the patient should be warned of these risks before the treatment is begun.

Post-partum necrosis of the anterior lobe of the pituitary

Sheehan and Murdoch have published a series of interesting investigations by which they claim to show that post-partum ischaemic necrosis of the anterior pituitary is relatively common in cases of obstetric shock and collapse, especially from post-partum haemorrhage. This condition was found at necropsy in 13 out of a series of 46 women who died in the puerperium, but who survived for a period of at least 14 hours after child-birth. This minimal survival time is required for the evolution of the lesion into a visible form.

Sheehan and Murdoch, in a follow-up of 128 women who had had more or less severe haemorrhagic collapse at childbirth, found that in 41 there were symptoms suggestive of anterior-pituitary deficiency. Amongst these symptoms sexual hypofunction, amenorrhoea or oligomenorrhoea was common, and Sheehan and Murdoch believe that their syndrome is identical with the condition described under the name of 'superinvolution of the uterus' by A. R. Simpson in 1883. The authors believe that Simmonds's disease corresponds to this condition in its extreme form.

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DISEASE IN CHILDREN

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'The older I grow the more hopeful I grow,' said Sir James Goodhart towards the end of his life when seeing in consultation a very sick child. This must be the experience of most who have watched the progress of paediatrics during the past fifty years. This optimism has a sound basis not only in the recuperative powers of childhood, but in the progress which has been made in every department of medicine which concerns children.

ADVANCES IN ANTENATAL CARE

Even from the stage of intra-uterine existence the outlook for the individual as regards life has improved. A quarter of a century ago the importance of special care of the prospective mother was beginning to be realized as having for one of its objects the safeguarding of the life and health of the coming child. Since then more and more attention has been given to this aspect of preventive medicine, antenatal clinics have been established in many of the larger towns and, by the teaching of antenatal care to students in teaching hospitals, the practitioners in rural districts are becoming better equipped to give advice and treatment to expectant mothers, so that mal-positions *in utero*, syphilis in the mothers, and other conditions endangering the life or health of the coming child can be recognized and treated.

Probably as a result of this antenatal care there has already been a diminution in the proportion of still-births. In 1858 Dr. T. H. Tanner stated that in the chief cities of Europe the proportion of still-births was 1 in 22 births, approximately 45 per 1,000. Twenty-five years ago when antenatal care was just beginning to be recognized in this country as a factor in public health, the proportion of still-births to total births in England and Wales was 40 per 1,000; the last available (quarterly) return in 1938 showed 37 per 1,000.

That still-births are related in some degree to social environment, to poverty and distress, seems likely from the very high figures which come from South Wales, where the proportion in recent years has often been 49 to 54 per 1,000 births, in contrast with Greater London where it has been 32 to 34 per 1,000. These figures suggest that with improvement of social conditions, with a revival of industry and a wider application of antenatal care, still-births might be further reduced in all parts of the country.

REDUCTION OF INFANT MORTALITY

But whilst the chances of health and live birth have slowly increased for the infant *in utero*, the prospect for the live-born infant has been improving almost from year to year. A century ago, in 1839, the proportion of infants dying within the London area, 'within the Bills of Mortality', under the age of two years to those christened in that year (the only means of reckoning at that time) was approximately 250 per 1,000; in 1937 the proportion of deaths under two years of age to the total births in that year in England and Wales

was approximately 15 per 1,000. These figures are only roughly comparable, but they give some idea of the enormous improvement which a century has produced in the outlook for the new-born infant.

With the more accurate figures available since the registration of births and deaths became general, and in 1874 compulsory, it is possible to appreciate more clearly the changed outlook for the infant. It was estimated that from 1866 to 1870, out of every 1,000 infants born, 157 died in the first year; in 1899 the number was 163; in 1909 it was 109, in 1919 it was 89, in 1929 it was 74, and in 1937, the last full figures available, it was 58 per 1,000 live births in England and Wales.

To those who remember the diarrhoeal mortality amongst infants forty years ago—and this was one of the largest factors in the heavy infantile mortality of those days—the present-day saving of infant life appears as light after darkness.

Infant feeding

Infant feeding has passed through many fads and phases since then, but probably the introduction of dried milk and the spread of knowledge as to the importance of clean milk and as to the safeguard of pasteurizing milk, have played a large part in reducing infant mortality, whilst the inauguration of Infant Welfare Centres and Schools for Mothers since the early years of this century, and particularly since 1906, has done much to increase the child's chance of life and health. It is noteworthy that the rapid fall in infant mortality dates from about that time.

Mortality of illegitimate children

Although there is cause for satisfaction in the general improvement in the infant's prospect of life, there is grave reason for dissatisfaction with regard to the fate of illegitimate infants. No inborn difference of viability will account for the fact that whilst, for example, in 1936 the deaths per 1,000 births in England and Wales were, amongst the legitimate, 60, they were amongst the illegitimate 103; and in 1937 amongst legitimate 56, illegitimate 88. This disproportion is even more marked when only Greater London is considered; in this heavily populated area in 1937 the mortality under one year per 1,000 births was amongst the legitimate 51·02, amongst the illegitimate 114·58.

One factor, comparatively small it is true, but important because it is entirely preventable, contributes to this disproportionate mortality amongst the illegitimate, namely, overlying. In 1915 the Registrar-General pointed out that deaths from this cause were four times as many in the illegitimate as in the legitimate. These cases are now included under the heading 'Suffocated in bed or not stated how'; in 1936 there were included thus of infants under one year of age per 1,000 live births in England and Wales, 0·4 legitimate, 1·0 illegitimate, and in 1937 0·38 legitimate, 0·87 illegitimate, so that the proportion of illegitimate to legitimate babies dying from this cause is still about 2·5 to 1.

In respect of this item of infant mortality there can be no inherent difference between the child born in wedlock and the child of the unmarried mother, and it is equally impossible to attribute the greater prevalence of overlying in the latter to chance. It can only be hoped that with increasing care of the unmarried mother there may be a better chance of survival of the innocent but unwanted child.

Rickets and vitamins

One of the most striking advances in the improvement of child-health has been the diminution in the prevalence and in the severity of rickets in the last thirty years. In 1907 out of 163,253 deaths in England and Wales under

the age of 5 years, 1,235, i.e. approximately 7·6 per 1,000, were attributed to rickets; in 1937 the comparable figure was 3·1 per 1,000. In London the severe cases of rickets which were common in children's out-patient departments forty years ago have become almost a rarity.

Probably this improvement in respect of rickets has been a factor in reducing the mortality from bronchitis and various forms of pneumonia. In 1887 these affections accounted for 13·5 per 1,000 of the deaths under five years of age in England and Wales; in 1937 they accounted for only 4·6 per 1,000. Certainly in the days when severe rickets was common any pulmonary complication was of the gravest outlook.

The recognition of vitamin D as a factor of importance in the normal development of bone, and also the more recent knowledge of its mode of action in promoting the utilization of calcium and phosphorus, has had some share in the diminution of rickets, by emphasizing the need for a diet which contains both the vitamin and the particular salts in sufficient quantity. The formation also of vitamin D in the body by the action of sunlight and of the ultra-violet rays in sunlight has become widely recognized, and this knowledge has further contributed to the reduction of rickets.

But, as in the case of the other vitamins, there has been a tendency to over-stress the risk of deficiency. It is evident that only minimal quantities of the vitamins are needed. Nature has been careful that the things upon which life and the continuance of the race depend shall not easily be at fault, and though we have wandered more and more from the ways of Nature, in one at least of her provisions she still affords the necessary protection, to wit, in breast milk. The mother's milk still has its protective powers, even though the mother be fed upon a very ordinary mixed diet, perhaps even a poor one; it is not merely a work of supererogation but sometimes a source of digestive trouble to give a breast-fed infant orange juice, and cod-liver oil or halibut-liver oil or the like, as if these were a necessity and Nature were becoming effete.

It has yet to be shown that there is any advantage from exceeding the minimal amount of vitamins required. In so far as storage is possible this may be a justification for generous provision of vitamins, but there is certainly no ground for supposing and, so far as clinical experience goes, no warrant for the assumption that the more vitamins a child has, the healthier it will be.

To the artificially-fed infant in these days of dried milk and heated milk, an additional supply of vitamins is a necessity, and the wide-spread knowledge of this has undoubtedly reduced the frequency of rickets and almost abolished the occurrence of scurvy.

It may, however, be suspected that the aetiology of rickets is not quite so simple as the recognition of vitamin D at first suggested. There are undoubtedly cases in which a liberal supply of vitamin D neither prevents nor cures rickets, although the diet seems to be adequate in other ways. The remarkable cases of renal rickets, in which no amount of cod-liver oil or halibut-liver oil or other substances rich in vitamin D prevents or cures, although the serum shows an adequate supply of calcium and phosphorus, sufficiently demonstrate that, if these bone changes with renal disease are really rickets, vitamin D is not *per se* curative of rickets; there are factors in metabolism which are at present not fully understood.

Tuberculosis

An optimism which looks for still further improvement is justified by the decrease which has occurred in the mortality from tuberculosis in children under five years of age during the past half-century. In 1887 the proportion of deaths due to tuberculosis of all kinds at this age was approximately 75 per 1,000 in England and Wales; in 1927 it was 43 per 1,000 and in 1937 it was 31 per 1,000.

Amongst the many factors which have contributed to this decrease of the

mortality from tuberculosis in the first five years of life—the quinquennium of childhood in which most deaths from tuberculosis occur—probably improved housing and better feeding and a wider appreciation of the value of fresh air have been specially potent, but the more general use of pasteurized or dried milk for children must also have done much to reduce the number of deaths due to tuberculous meningitis, tuberculous peritonitis, tabes mesenterica, and the occasional spread from cervical glandular infection. In all these respects still further improvement may be expected with advancing improvement in social conditions and increasing knowledge of the simple laws of health, particularly of the saving value of fresh air and open air and of the needless danger of unheated milk, especially during the first seven years of life.

Syphilis

Amongst the scourges of childhood half a century ago one of the most deplorable— inasmuch as the child was suffering for the actions of its parents—was syphilis with all its years of disability and disfigurement, even if the child had escaped with its life in the pre-natal and neonatal periods.

It is difficult to estimate its frequency, for only the fatalities are on record, but clinical experience makes it quite certain that in this country the typical manifestations of congenital syphilis in children beyond the age of infancy are far less frequent than they were and are becoming more and more rare. Effective treatment of the parents before the birth of the child now often results in the birth of a healthy child when formerly there would have been a miscarriage, a still-born child, or a live-born heavily infected infant.

So far as mortality figures can give any idea of the decrease in congenital syphilis, the following show the steady fall which there has been in the mortality from this cause amongst infants under one year of age in England and Wales during the last fifty years:

TABLE I.—Deaths from congenital syphilis
per 1,000 live births

1887	—	—	—	—	1·78
1907	—	—	—	—	1·23
1927	—	—	—	—	0·77
1932	—	—	—	—	0·47
1937	—	—	—	—	0·23

What proportion of still-births should be added to these figures is impossible to say, but it is evident that within this period the mortality has fallen to less than one-seventh of the figure at the beginning—a decrease which is largely due to the introduction of the Wassermann test, the use of the various arsenicals, and the establishment of special clinics for the treatment of venereal diseases.

Sulphanilamide

In respect of drug treatment there has been less solid advance than in hygienic prevention, but the recent introduction of the sulphanilamide preparations has undoubtedly provided a valuable means for combating streptococcal infection and evidence seems to be accumulating that preparations of this group may also be effective against pneumococcal and meningococcal infections. It is a great advantage in any drug that is to be used for children that it should be efficient when given orally, so that the discomfort and alarm of injections may be avoided; the earlier preparations of the sulphanilamide group were found to be so much less potent when given orally that it was often necessary to supplement oral administration by intramuscular injection. Later modifications have been found to be almost if not quite as effective

when given by mouth as when administered intramuscularly or intrathecally. It has been stated that preparations of the sulphanilamide group are of value in *Bact. coli* pyelitis; but it may be doubted whether, even if this is so, their use is advisable for this affection, inasmuch as all this group of drugs are liable to produce toxic effects, a risk which may be worth taking when no equally efficient and less toxic treatment is available; in the case of acute *Bact. coli* pyelitis in infants a perfectly effective and harmless remedy is available in potassium citrate properly used. For the more chronic *Bact. coli* infections of the urinary tract mandelic acid in the form of the ammonium salt, a drug recently introduced, has proved of value and probably less troublesome to the patient than the ketogenic diet which was in use a few years ago and certainly sometimes gave strikingly good effects.

Specific fevers

There is another direction in which not only has advance already been made both in prevention and in treatment, but the expectation of further progress seems well justified, namely in regard to specific fevers.

The introduction of antitoxin treatment forty-five years ago at once reduced the mortality of diphtheria. Up to that time diphtheria was the cause of death in about 800 per million annually of the child population under fifteen years of age in England and Wales; by 1907 the proportion had fallen to 541, and during the last twenty years has ranged from about 250 to 400; in 1937 the proportion was 310. But it is on prevention that hopes have been concentrated in recent years, especially since the introduction of the Schick test. Immunization of Schick-positive children, whether actively with A.P.T. (alum-precipitated toxoid) or with T.A.F. (toxoid antitoxin floccules) or passively with antitoxin, reduces the incidence of the disease though it may not entirely prevent it; the immunized cases also, even if affected by this disease, usually suffer less severely than those not so protected. A combination of active and passive immunization, recently tried in France, may prove to be still more effective.

None of these methods ensures absolute security, for it would seem that even in a Schick-negative child severe and fatal diphtheria may occur, but this is very exceptional. Immunization of school-children, not being compulsory, is only gradually coming into wider use so that as yet figures hardly give any idea of its value; moreover as the mortality generally falls most heavily on the pre-school age, propaganda directed to the school age leaves this period of special susceptibility untouched. With increasing appreciation by parents of the value of immunization, it may be hoped that children, both in the pre-school and in the school period, will suffer less with diphtheria and that the number of deaths from this cause—2,770 children under fifteen years of age in England and Wales during 1937—may be much further reduced.

Immunization may be said to have proved its value beyond doubt in the case of diphtheria, but less certainty can be claimed for similar methods of treatment in measles, scarlet fever, and whooping-cough. Serum whether from adults who have had measles some years previously or from convalescent cases has been used in epidemics of measles, and recently an 'immune globulin' prepared from the human placenta has also been tried with apparent success in reducing both the spread of measles and its severity. The introduction of the Dick test has provided a method of determining the susceptibility of individual children to scarlet fever, and passive immunity can be given by intramuscular injection of an antiscarlatinal serum.

These methods have been used with apparent advantage when epidemics have occurred in institutions, such as schools. It is difficult, however, to estimate what weight should be attached to figures of individual epidemics as showing the results of such treatment. From unknown causes epidemics vary in their severity and their spread; there has also been a striking and

steady fall in the mortality of all the common specific fevers, namely diphtheria, measles, scarlet fever, and whooping-cough in children in this country during the past fifty years, and this steady decline in the mortality began many years before these methods of testing susceptibility and of immunization were introduced, so that it can only be concluded that other factors have contributed to the improvement. Amongst these it may be conjectured that improved sanitation, especially by better housing with less overcrowding, and better nutrition, and in recent years more careful supervision of the general health of the child, have played an important part.

These factors, however, do not detract from the importance of the direct methods of defence by these recent prophylactic measures against the still serious inroads of the specific fevers.

Amongst diseases which at times become epidemic, poliomyelitis is one of the most disastrous—not in its actual mortality, which is comparatively small, but in its crippling effects. In 1937 the total number of deaths from poliomyelitis in England and Wales in children under the age of 15 years was 74; in 1936 it was 63. In contrast with these figures is the much larger number of those permanently disabled in greater or less degree every year. The average number of cases of poliomyelitis notified annually in England and Wales, at all ages, is about 600, and, as it is very exceptional for recovery to occur without leaving some permanent paralysis or weakness, it is evident that hundreds are more or less crippled every year as a result of this disease.

The value of convalescent serum for immunizing children who have been in contact with the infection or are in a place where the disease is occurring is still regarded as questionable, and a vaccine has proved useless. When once the disease has attacked a person any immunizing agent to be of any value must take effect before paralytic symptoms begin to appear, and for this reason it has been stated that the only route by which the nerve-cells could be reached and protected sufficiently rapidly is the intravenous. The virus, however, seems to reach the nerve-cell so quickly that, according to most observers, no serum of any sort, however administered, is of any use after the first symptoms of the disease appear. It may, however, be doubted whether this rule may not have exceptions. There are cases in which the paralysis, instead of appearing almost simultaneously in several parts of the body, attacks first one limb and then after an interval, it may be of three or four days or even weeks, attacks another limb; it seems possible that in these rather exceptional cases there may still be an opportunity for checking the activity of the virus by some immunizing agent given at the first onset of the disease, so that at least some of the later spread of the paralysis may be prevented.

ALIMENTARY TRACT DISEASES

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UPPER DYSPHAGIA AND ANAEMIA; PATERSON'S (SO-CALLED PLUMMER-VINSON) SYNDROME

The fully developed syndrome of upper dysphagia with anaemia and atrophic glossitis is rare, but, if women with simple achlorhydric anaemia are questioned about their swallowing, it is remarkable how frequently they admit that they experience slight difficulty in the region of the upper oesophageal sphincter. There is no doubt that D. R. Paterson of Cardiff was the real discoverer of the syndrome of upper dysphagia with anaemia. He described it in the *British Medical Journal*, in 1906, and more fully in an issue of the *Journal of Laryngology*, in 1919, which also contained a paper by Brown Kelly on the same subject.

In 1914 Plummer independently observed the condition, but, so far as I know, did not write about it, and Vinson, his colleague at the Mayo Clinic, published an article on the subject in 1922; both regarded it as hysterical in origin.

In 1926 I described a case in *Guy's Hospital Reports*, and showed that there was no justification for regarding the condition as hysterical. As I was familiar with Vinson's paper, but had not seen Paterson's and Brown Kelly's, I referred to it as the 'Plummer-Vinson syndrome', an unfortunate name which has become widely adopted both in Great Britain and in America. The disease should obviously be known as 'Paterson's syndrome' if 'upper dysphagia with anaemia' is regarded as too long a name.

In severe cases the atrophy of the mucous membrane of the tongue and pharynx is accompanied by atrophy of the lips, leading to a gradual contraction of the oral aperture, with cracks at the corners, and atrophy of the nails, which become thin and spoon-shaped. The atrophy is a direct result of iron deficiency, as Waldenstrom has shown that it can be cured by the administration of iron, even in the exceptional cases in which it is not associated with anaemia. The forced passage of an oesophagoscope or mercury bougie into the oesophagus generally leads to immediate and permanent relief from the dysphagia.

Paterson was the first to point out that this disease predisposed to epithelioma at the pharyngo-oesophageal junction, both conditions being almost exclusively confined to women, whereas carcinoma of the middle and lower end of the oesophagus is much more common in men. A large majority of cases of epithelioma in this situation give a long history of upper dysphagia with anaemia, the adequate treatment of which can be regarded as a true prophylaxis of cancer (Hurst, 1939).

SIMPLE ULCER OF THE OESOPHAGUS, AND SHORT OESOPHAGUS

Friedenwald and Chevalier Jackson were the first clinicians to recognize the comparative frequency of oesophageal ulcer, but, in 1929, it was still

generally regarded as a pathological curiosity. Before that year we had never made the diagnosis, but since then we have seen eight certain and an additional five probable cases at New Lodge Clinic alone, no less than six in the first half of 1939. This is due to the fact that we have gradually come to recognize the very characteristic clinical picture that oesophageal ulcer presents.

The ordinary routine X-ray examination almost always fails to show anything abnormal, but, when its presence is suspected, examination with a special technique generally reveals a definite 'niche' at the extreme lower end of the oesophagus immediately above the cardiac sphincter. A narrowing of the lumen caused by spasm is often present just above the ulcer, but the sphincter is relaxed and widely open. The diagnosis can always be confirmed by oesophagoscopy.

Clinical picture

Pain is felt under the lower end of the sternum whilst swallowing insufficiently chewed lumps of food, various other articles of diet, and alcohol. It is also felt in the same situation an hour or two after meals, if the patient bends forward or lies down. Relief is afforded by alkalis. Hyperchlorhydria is generally present. The stools always contain occult blood, and haematemesis may occur. A clinical diagnosis of gastric ulcer has generally been made, but this has subsequently been rejected when X-rays have failed to reveal any abnormality.

Association with short oesophagus

We have found that oesophageal ulcer is almost always associated with that form of hernia of the upper part of the stomach through the diaphragm which is caused by a congenitally short oesophagus (Briggs, Dick, and Hurst). A small diaphragmatic hernia of this kind is often missed in a routine X-ray examination, when recognized, any associated symptoms are generally ascribed to inflammation or ulceration of the herniated portion of the stomach instead of to their true cause—an oesophageal ulcer.

X-ray findings

Both the ulcer and the hernia can be demonstrated by examining the patient in the horizontal position. The barium sulphate emulsion is best taken in this position, but alternatively the contents of the stomach can always be forced through the sphincter into the lower end of the oesophagus by pressure exerted on the abdomen. The cardiac sphincter appears to be permanently relaxed when the oesophagus is abnormally short and a portion of the stomach is above the diaphragm, in contrast with the normal condition in which it is closed, except when relaxation occurs in the last stage of deglutition.

The stratified epithelium of the oesophagus is unable to resist the eroding action of regurgitated gastric juice, especially when the acidity is high. A superficial erosion forms and in course of time develops into a chronic ulcer the healing of which may ultimately produce a fibrous stricture and dysphagia. There is some evidence that carcinoma of the lower end of the oesophagus occasionally develops from malignant degeneration of a simple ulcer.

Treatment

The treatment of oesophageal ulcer consists in giving a pint of milk with additional cream four times a day. It should be drunk in the erect position, and the last feed should be given at least three hours before going to bed. A quarter of an hour after each feed some water and orange-juice should be drunk to wash away any traces of milk sticking to the mucous membrane. If the pain is severe, or dysphagia is present, atropine and olive oil should

be given a quarter of an hour before the feeds. The head of the bed should be raised on blocks to prevent regurgitation of gastric juice into the oesophagus during the night.

The treatment should continue until occult blood disappears from the stools, X-rays show no ulcer crater, and the oesophagoscope shows a normal mucous membrane. The patient is then given a post-ulcer regime similar to that prescribed for patients with gastric or duodenal ulcer and should continue to sleep with his thorax higher than his abdomen.

ANOREXIA NERVOSA

Aetiology

Both in America and on the Continent anorexia nervosa is generally regarded as an endocrine disorder allied to Simmonds's disease. There is no scientific support for this view, and the invariably rapid recovery which follows well-conducted psychotherapy is in striking contrast with the failure to benefit from any form of endocrine therapy. There are two symptoms which might at first appear to support the endocrine theory—the amenorrhoea, which constantly accompanies the anorexia in the girls and young women who are the most frequent sufferers from the disease, and the remarkable development of downy hair over the face, limbs, and body. The amenorrhoea cannot be caused by any deficiency in the diet, as its onset may coincide with, or even precede, that of the anorexia, and it always persists for a time, sometimes for a year or longer, after recovery is otherwise complete. There is good reason to believe that the amenorrhoea, like the anorexia, is psychogenic, and there is no doubt that amenorrhoea without anorexia may follow emotional disturbances. The hairiness is a direct result of starvation. It is a constant feature in the emaciation which occurs in periods of famine, and it disappears as nutrition improves.

Treatment

It is clear that the logical treatment of anorexia nervosa is to reverse the process which gave rise to it, and to overcome the anorexia by persuading the patient to eat. It is quite unnecessary in the early stage of treatment to deal with the primary psychological troubles, and such accessory treatments as the use of pituitary or ovarian extracts, insulin, vitamins, or special diets, are also quite unnecessary. Treatment is extremely difficult in the patient's home, and hardly less difficult in the general ward of a hospital, but it is comparatively easy in a nursing home. We have had the opportunity of treating 58 cases at the New Lodge Clinic since 1921, and without exception they have done well.

The patient is made to realize that the physician fully understands her difficulties. She is told that, in spite of her nausea, loathing of food, and discomfort on eating, she must eat, as it is only by eating that she can re-educate her appetite. It was lost by fasting; it will be restored by eating. The process will be uncomfortable, but it can, and must, be carried through. After one long conversation, a full meal is given, and the patient is not left until the whole of it has been consumed. There must be no time limit for this first meal; resistance is often extreme, but it can always be overcome with patience and good temper. After success with the first meal progress is generally uninterrupted. Resistance still occurs in many cases, but it becomes rapidly and progressively less. In a severe case it may be necessary for the physician to be present at one meal a day for the first week or fortnight, but the management of the remaining meals may be left to an experienced nurse.

When the appetite is returning and the patient is eating full meals without difficulty, the psychological problems which led to the anorexia may be discussed, but this is not always necessary, as in many instances they have

been forgotten in the severity of the illness that followed, or they have solved themselves by the time the patient has come under treatment. A few straightforward conversations are sufficient to reveal and straighten out most mental tangles. No form of deep analysis is ever required.

Prognosis

The ultimate prognosis is excellent, and I have never seen a case in which the cure of the anorexia was followed by the substitution of some other hysterical symptoms. Several of our cases date from ten or fifteen years ago, and so far as I know there has been no recurrence.

TREATMENT OF GASTRIC AND DUODENAL ULCER

The recent investigations of Davidson and Nicol by fractional analysis continued throughout the day in duodenal ulcer patients on various diets have thrown doubt upon the value of the usual dietetic and drug treatment of ulcer. They have shown that hourly feeds produce less complete neutralization in patients with duodenal ulcer and hyperchlorhydria than two-hourly feeds, and that the latter produce less neutralization than feeds containing a more liberal selection of food. On the other hand, a continuous drip administration of 5 fl. oz. of milk per hour through a tube produces a much greater degree of neutralization than any other diet.

In spite of these unexpected results I am still convinced that hourly feeds of 5 fl. oz. of milk or milky feeds is the best diet for ulcers until healing is complete. Whatever its effect on the acidity may be, the experience of large numbers of patients who have previously had two-hourly feeds shows that they get much more rapid and complete relief from their symptoms with hourly than with two-hourly feeds. With two-hourly feeds it is very common for pain to occur at the end of $1\frac{1}{4}$ or $1\frac{1}{2}$ hours, and this can be prevented by taking a feed at the hour. Even with hourly feeds pain is sometimes experienced after 45 or 50 minutes. This can be prevented by instructing the patient to take his feeds very slowly, allowing $\frac{1}{4}$ to $\frac{1}{2}$ an hour to elapse before they are completed. By this means a considerable degree of neutralization of acidity would presumably be secured.

The main reason for excluding any fish or chicken from the diet till healing is complete is that the best indication of the progress of a case is the result of a very delicate test for occult blood. The combination of the guaiacum reaction with spectroscopic examination introduced by Ryffel and Payne is so delicate that even a small quantity of fish or chicken gives a positive chemical reaction and a haematoporphyrin spectrum; the reaction remains positive in most cases until after the ulcer crater has disappeared radiographically. Gastroscopy shows, however, that healing of a gastric ulcer may be delayed for about a fortnight after the occult blood tests become negative. Our routine now is to examine the stools for occult blood on alternate days and to repeat the X-ray examination fortnightly. The repeated X-ray examination is important in gastric ulcer, especially in the prepyloric region, as, if progressive improvement does not occur, even if the symptoms have disappeared, the suspicion of malignant degeneration requires consideration, and a partial gastrectomy should be performed without further delay.

With duodenal ulcer the strict treatment should be continued until a fortnight after both tests are completely negative. With gastric ulcer gastroscopy is performed when the occult blood has disappeared and the X-rays show no niche; in most cases healing is found to be incomplete, and further strict treatment is required before complete cicatrization occurs. The importance of ascertaining when healing is complete lies in the fact that in the past the strict treatment of ulcer has been much too short, and so-called recurrences are really relapses, the ulcer having become latent, though unhealed. When

healing is really complete, permanent adherence to a suitable post-ulcer regime after a month on an intermediate diet, with gradual return to full physical and mental activity, will prevent a recurrence in the large majority of cases.

The experiments of Davidson and Nicol have also thrown doubt on the efficacy of antacids, such as magnesium trisilicate, and of atropine, as these authors found such drugs had no effect in reducing the acidity in hyperchlorhydria. This does not agree with the results obtained from experiments with single test-meals by many observers in the past, but they call for careful scrutiny as investigations by continuous fractional analysis accord much more closely with natural conditions. Here again, however, clinical experience shows that magnesium trisilicate and other antacids invariably relieve pain occurring between meals, and that atropine in maximal doses is the most effective substance for treating the severe pain which in exceptional cases continues in the early stages of treatment, especially at night.

TREATMENT OF HAEMATEMESIS

The treatment of haematemesis by immediate feeding, as first recommended by Holmgren and recently popularized by Meulengracht, is founded on the assumption that when death occurs it is largely a result of malnutrition. But Ryle and I (1937) concluded from an extensive inquiry that the mortality from haematemesis when treated by the old-fashioned methods of rest with a short period of starvation and with morphine is extremely low. In most of the rare fatal cases there had been no prolonged period of starvation, and post-mortem examination showed that a large sclerotic artery with a hole in it was exposed, a condition which could not conceivably have reacted any better to a full diet than to starvation. The only treatment which might have saved the patients would have been the direct surgical treatment of the ruptured artery, preferably by excision of the ulcer, with or without the greater part of the stomach, although in each of the three cases of mine in which it had been decided to do this the technical difficulties proved insuperable and the patient died.

Transfusion should be carried out when the haemoglobin is below 30 per cent. Under ordinary conditions it is best to give a small transfusion, and to repeat it as often as necessary if the bleeding continues. In hospitals, and wherever else the treatment is available, severe cases should be given the benefit of continuous drip transfusions of sufficient blood to raise the haemoglobin to the normal level, a treatment which gives excellent results (Avery Jones).

GASTROSCOPY

The invention of a flexible gastroscope by Schindler has added a method of investigating gastric disorders of the greatest value (Schindler; Moutier; Henning). It can be passed without danger and with surprisingly little discomfort to the patient. I now regard it as an essential part of the investigation of any patient in whom disease of the stomach is suspected but in whom radiography leaves doubt as to the exact diagnosis. Apart from cases in which a test-meal shows the presence of achlorhydria and excess of mucus in every fraction and in those in which grossly thickened folds can be seen with X-rays, it is the only reliable means of diagnosing gastritis. Those who have long believed that gastritis is very common and very important have had their belief completely confirmed by gastroscopy. The diagnosis is not of merely theoretical importance, as most cases of gastritis can be cured by suitable diet and lavage, whereas in the past a diagnosis of nervous dyspepsia has too often been made in such cases with the result that treatment, though often temporarily efficacious, never resulted in permanent relief. Moreover, the

diagnosis and successful treatment of gastritis are likely to reduce greatly the incidence of cancer of the stomach, which is probably caused by malignant degeneration of the chronically inflamed mucosa in about 70 per cent of cases.

Gastroscopy often reveals the cause of haematemesis in cases in which X-rays have not revealed an ulcer. Most commonly it is a result of erosions associated with gastritis. Aitken and Rodgers (1939) have described a form of subacute ulceration associated with achlorhydric gastritis which is too superficial to form a niche recognizable by radiography. Lintott and I found that treatment of the associated gastritis in such cases leads not only to healing of the ulcer but to restoration of gastric secretion, even when the original achlorhydria is refractory to histamine. Douthwaite and Lintott have shown how gastroscopy can throw light on the effect of drugs and other irritants on the stomach. Their discovery of the irritant effect of aspirin on the gastric mucosa was followed by the observation of actual haemorrhage around fragments of aspirin in a patient who had had a number of attacks of unexplained haematemesis and who habitually swallowed several whole aspirin tablets for the relief of migraine (Hurst and Lintott). It seems probable that aspirin may be a common cause of unexplained haematemesis.

Recurrence of gastric ulcer is likely to become very rare if gastroscopy is always used before discontinuing strict treatment after occult blood has disappeared from the stools and X-rays no longer show any sign of activity. Observations of this kind show that two or three additional weeks are generally required before the granulation filling the ulcer crater is replaced by a scar. In the past so-called recurrences have generally been relapses of incompletely healed ulcers (see p. 46).

When clinical, radiological, and biochemical observations leave a doubt as to the diagnosis in a case of dyspepsia, gastroscopy is often of value either in excluding any serious organic disease or, less often, in revealing an early carcinoma.

It is quite common for haemorrhage to occur after gastro-jejunostomy from superficial ulcers or erosions of the gastric mucous membrane bordering on the stoma after a gastro-jejunostomy, and even chronic gastro-jejunal and jejunal ulcers are often difficult to recognize with certainty by X-rays. With the gastroscope it is almost always possible to get a good view of part or all of the anastomotic ring and by this means to make an accurate diagnosis of the cause of symptoms following an unsuccessful gastro-jejunostomy. Gastroscopy has confirmed the view I had held for many years—that severe inflammation with or without superficial ulceration may be present in the region of the anastomosis even when X-rays show no abnormality and inspection and palpation at an exploratory laparotomy reveal nothing or only ‘adhesions’. As with gastric ulcer, gastroscopy is the only satisfactory means of determining when recovery is complete and active treatment no longer necessary.

BILIARY DRAINAGE IN THE DIAGNOSIS OF GALL-BLADDER DISORDERS

The diagnosis of disorders of the gall-bladder was revolutionized by the introduction of cholecystography by Graham and of biliary drainage by Lyon. By means of cholecystography gall-stones and the more severe forms of cholecystitis can often be diagnosed, but the much more common cases of mild cholecystitis escape recognition. On the other hand, biliary drainage brings confirmation and precision to the diagnosis of gall-stones and severe cholecystitis, and without it a definite diagnosis of the milder forms of cholecystitis is impossible. I have no hesitation in regarding biliary drainage as an even more valuable diagnostic method than cholecystography, and it is therefore a constant source of surprise to me that it should still be used so rarely in England.

Under normal conditions a free flow of bile is obtained by injecting 25 c.cm. of a 25 per cent solution of magnesium sulphate through a duodenal tube. If no flow of dark bile is obtained it can be assumed that the contents of the gall-bladder are unable to reach the common bile duct; under these conditions no shadow of the gall-bladder can be obtained with cholecystography. If, however, a good shadow is present, Lyon's test should be repeated, the negative result being probably due to the tube not having reached the duodenum. Alternatively, if a good flow is obtained but no shadow is present, cholecystography should be repeated, as a negative cholecystogram is not compatible with a positive Lyon's test. Normal bile may give a small deposit of mucus but should contain no cells, pigment granules, or cholesterol crystals, and cultures should be sterile. The presence of excess of mucus with groups of columnar epithelial cells indicates catarrhal cholangitis, in severe grades of inflammation leucocytes are present and in rare cases red blood corpuscles. Pigment granules are also often found when the gall-bladder is inflamed. Except in the mildest form of catarrhal cholangitis cultures yield *Bact. coli* and much less often other organisms, such as enterococci, staphylococci, and various non-lactose fermenting bacilli, including *Bact. typhosum* and *paratyphosum*. In rare cases enormous numbers of actively moving *Lamblia* are found.

Knott has pointed out that cholesterol crystals may occur in two forms. Small perfectly formed crystals may be deposited from bile in which there is either excess of cholesterol or deficiency of the solvents of cholesterol (bile salts); this indicates the desirability of giving a cholesterol-poor diet as prophylaxis against the development of gall-stones. In other cases large cholesterol crystals with the corners broken or rounded are found, these come from the surface of gall-stones and their presence is pathognomonic of cholelithiasis. If no other abnormality is present it can be assumed that the gall-stones are not associated with active cholecystitis; if associated with excess of mucus, epithelial cells, and perhaps leucocytes, and especially with pigment granules, and if cultures yield *Bact. coli* or other organisms, cholecystitis is certainly present as well.

Droplets of yellow lipid material may be found in the bile. This has a similar significance to the presence of small cholesterol crystals and is often associated with the so-called strawberry gall-bladder. In most cases there is no evidence of any accompanying cholecystitis.

It is always necessary to compare the bacteria of the duodenal contents obtained before injecting the magnesium sulphate with those of the bile obtained after the injection so as to make certain that any organisms found in the latter are derived from the bile itself and are not due to an independent infection of the duodenum. This is especially important in cases of achlorhydria, in which the duodenum is almost always infected with *Bact. coli*. If the number of organisms in the bile greatly exceeds the number in the duodenal specimen or if the latter is sterile, their biliary origin is assured. To make the matter still more certain the duodenum should always be washed out with sterile water after a sample of its contents has been obtained and before the magnesium sulphate is injected.

REGIONAL ILEITIS

Now that Crohn's work on regional ileitis is becoming more widely known in England, the disease is being diagnosed with steadily increasing frequency. Until this year, however, no case in which a fistula had developed had been recorded outside America, although Crohn had described this as a comparatively common complication. I have recently published an account of three cases in which fistulae were present (Hurst, 1939). In the first, multiple fistulae had formed between ileum and ileum and ileum and colon, and recovery

followed excision of the affected ileum with closing of the fistulae. In the second, a localized abscess developed, together with extraperitoneal blind fistulae, in a woman of 74; although no operation was performed, she was still comparatively well and active two years later. In the third, the disease had spread from the terminal ileum to the rectum, where fistulae involving the peri-anal skin had formed; recovery followed excision of the peri-anal tissues and opening of the fistulae without any surgical treatment of the terminal ileum.

Bowen and Day have published a case in which a necropsy was performed on a patient who died from an inoperable growth of her uterus nine years after an ileo-colostomy had been performed for obstruction caused by regional ileitis involving the terminal 22 cm. of the ileum. She had made a perfect recovery; her bowels acted regularly, she bore a sixth child, and she had no further symptoms until her abdomen became swollen owing to the development of a uterine tumour. In spite of the absence of symptoms, active inflammation was still present in the affected bowel, although no spread of the disease had occurred. The rest afforded by short-circuiting does not therefore necessarily lead to healing, so that excision is preferable to conservative treatment whenever the risk is not too great.

THE ABUSE OF PURGATIVES—A CLINICAL ENTITY

One of the commonest disorders of the present day is that which results from the abuse of purgatives. The patients complain of what they call constipation, but when asked for details they admit that their stools are always unformed, being either soft or liquid, and they may not have passed solid faeces for years. They are not in fact suffering from constipation, but from diarrhoea. Many have been told that they have colitis because of the presence of mucus in the stools, whereas in truth the mucus is the response of a still healthy mucous membrane to the irritant action of the purgative, because it disappears directly the latter is discontinued.

All have abdominal discomfort associated with flatulence and distension, and some have attacks of colicky pain. Many have had their appendix removed for these attacks, either with no result at all or with aggravation of their condition. In addition to the abdominal symptoms they always feel tired, have no appetite, and are frequently subject to headache. Some have been taking a comparatively small amount of purgatives, others gigantic doses, such as an infusion made from 30, 40, or even 60 senna pods every night.

Most of these patients begin to take purgatives on their own initiative because they think they are constipated, in many instances not because of any irregularity in the action of their bowels, but because their symptoms remind them of what they have read in advertisements for proprietary medicines, such as 'Your whole system is poisoned and you feel sour, sunk, and the world looks punk'. By taking the purgatives they hope for 'inner cleanliness and buoyant health'.

It is remarkable how rapidly the majority can be cured. They are deprived of their aperients, and at first given liquid paraffin or some non-irritating vegetable mucilage. Many already know from past experience that both their abdominal and general symptoms will disappear at once, but they have been afraid to persevere because of the almost universal belief in the dangers of constipation. The symptoms disappear because they are a result of the toxæmia caused by the artificial diarrhoea produced by purgatives, and not of constipation which may cause local discomfort and much anxiety to the patient but rarely gives rise to toxæmia, because hard dry faeces do not undergo bacterial decomposition.

A purgative upsets the delicate mechanism of the ileo-caecal sphincter,

which normally results in the complete digestion of food in the almost sterile small intestine and the absorption of the products without bacterial decomposition. When a purgative is taken, a good deal of semi-digested food passes through the ileo-caecal sphincter and fills the entire colon. The fluid faeces act as a perfect culture medium for bacteria which give rise to putrefaction of proteins, fermentation of carbohydrates, and decomposition of fats, the toxic products of which are absorbed. The liver is often able to render the toxins inert, and the kidneys to excrete what has escaped the liver, but, if either of these organs is inefficient, or if the purging is excessive or continued over long periods, toxic symptoms follow.

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DISEASES OF THE BLOOD-FORMING ORGANS

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DIAGNOSIS

The past few years have been notable for the advances made in precise methods of laboratory diagnosis. What may be called the mathematics of haematology, the determination of absolute values for haemoglobin saturation, red-cell volume, red-cell diameter, and red-cell thickness as well as a recognition of the normal ranges of these values, have become familiar to those engaged in clinical work and are now regarded as essential for investigating obscure and intractable anaemias.

A sedimentation-rate determination is now an integral part of a haematological examination, since it serves to differentiate anaemias with an organic basis from those, such as pernicious anaemia, which are due to a functional deficiency. The sedimentation rate may be corrected for anaemia (Hynes and Whitby). From the technical aspect, those anaemias for which the cause is obvious and which naturally respond to appropriate treatment present little difficulty.

The problems of diagnosis are concerned more with those anaemic states for which there is no apparent clinical explanation and which fail to respond to empirical treatment with blood-building substances. In such cases the haematologist is not content with an investigation of the peripheral blood, for this may fail accurately to reflect the true state of the bone-marrow tissue. Hence, for selected and difficult cases, an examination of the sternal bone marrow, by puncture of the bone or by trephine, has proved an invaluable procedure, more especially for establishing a diagnosis of aleukaemic leukaemia, aplastic anaemia, carcinomatosis of bone, myeloma, myeloid-sclerosis, and also for the diagnosis of latent parasitic diseases, such as malaria and kala-azar.

When laboratory facilities exist, peripheral blood or marrow may be examined by supravital staining methods (Whitby and Hynes), which enable identification to be made of difficult and sometimes diagnostic cells. The development of marrow examination has shown that aleukaemic leukaemia is far more common, both in adults and children, than was previously supposed and how frequently this disease is wrongly diagnosed as aplastic anaemia.

It is now realized that crude qualitative methods for the detection of fragility of the red cells may fail to give the diagnostic information so essential in obscure cases of haemolytic anaemia. Creed, who has perfected probably the best standardized quantitative fragility test, emphasizes also that anaemic persons may not exhibit minor, but nevertheless diagnostic, degrees of fragility until the anaemia is cured; this because anaemia, *per se*, protects the red cells against saline haemolysis.

The normal limits of blood bilirubinaemia have been accurately defined, and

the results are now expressed as mg. per 100 c.cm. rather than in van den Bergh units. The normal value is 0.31 mg. per 100 c.cm. with a variation of ± 0.03 mg. per 100 c.cm. (Mills and Mawson; King, Haslewood, and Delory.

The technique of the various tests which are used in the haemorrhagic diseases has also been rendered more accurate. There is now a standard technique for Hess's tourniquet test (Elliott), whilst the determination of bleeding time by Ivy's method (Ivy, Shapiro, and Melnick) is more informative and accurate than is Duke's method (Vol. II, p. 483). The serological test for glandular fever (Paul and Bunnell; Davidsohn), the agglutination of sheep's red cells, has been shown to be reliable and accurate. Glandular fever produces changes in the leucocyte count which are not infrequently interpreted as leukaemic. The importance of differentiating a benign disease from one with a hopeless prognosis scarcely needs emphasizing.

ANAEMIAS

The main advances in those dyshaemopoietic anaemias which are due to iron deficiency and deficiency of the liver principle have been in improvements in methods of treatment. It is now clearly recognized that there is no simple diagnostic blood picture, divorced from clinical findings, for either idiopathic hypochromic anaemia or for pernicious anaemia. Both diseases may be closely imitated by other clinical states. Chronic haemorrhage should always be excluded in any iron-deficiency anaemia, whilst a macrocytic anaemia suggestive of pernicious anaemia may also occur with nutritional, intestinal, hepatic, and endocrine disorders. Cirrhosis of the liver is now recognized as a cause of macrocytic anaemia, though there is usually not the well marked anisocytosis and poikilocytosis that are found in pernicious anaemia.

The anaemia of myxoedema has been extensively studied by Bomford, who has separated a macrocytic normochromic anaemia, which is regarded as the anaemia of uncomplicated myxoedema, from other more complex blood pictures that may be found in this disease and which are caused by a deficiency of iron or of liver principle superimposed on the anaemia due to thyroid deficiency. Thyroid is now regarded as a general metabolic stimulant rather than a specific haemopoietic factor.

Tropical megalocytic anaemia (Vol. I, p. 439), at one time thought to be due to a lack of extrinsic factor, is now attributed to complex nutritional deficiencies because the disease is curable with crude liver extracts, but not with concentrated and purified extracts that will cure pernicious anaemia.

The haemolytic anaemias have been investigated from the experimental aspect by Dameshek, Schwartz, and Gross, who have been able to imitate the characteristic haematological changes, namely, increased fragility, spherocytosis, reticulocytosis, and bilirubinaemia, by means of artificial haemolysins of immune-body type. Thus, there is a tendency to return to the view that diseases such as the acute hemolytic anaemia of Lederer, the paroxysmal haemoglobinurias, and the acquired type of haemolytic jaundice are due, not to infection or to inherent defects in the red cells, but rather to definite haemolysins. Even congenital acholuric jaundice seems likely to fall into this class, necessitating perhaps the abandonment of Haden's theory (Vol. II, p. 473). In haemolytic anaemias, especially blackwater fever, a new pigment, which has been named methaemalbumen, has been discovered (Fairley and Bromfield).

HAEMORRHAGIC STATES

Certain haemorrhagic states have been studied from the point of view of plasma deficiencies. In severe liver disorders, especially those associated with jaundice, the plasma prothrombin (Dam and Glavind; Illingworth)

has been found to be considerably reduced in those in whom there is a tendency to bleed at operation. Vitamin K is effective in the pre-operative treatment of such conditions. Recent studies on haemophilia (Pohle and Taylor, 1937, 1938) suggest that a plasma deficiency may be responsible for this disease. It has long been known that damage to capillary endothelium, from lack of vitamin C, is responsible for the haemorrhagic symptoms of scurvy. Vitamin P, known also as citrin or hesperidin, which is associated with vitamin C in nature, appears to enhance the action of vitamin C and to be useful in certain purpuric conditions, notably the symptomatic and Henoch types.

TREATMENT

The discovery that some anaemias have a nutritional or a deficiency basis which demands specific factors for treatment has led to the production of large numbers of proprietary preparations. Many of these consist of mixtures of iron, copper, liver extract, vitamins, and other potentially haematinic substances. Such preparations cannot be recommended for scientific work or for rational therapy; what they gain in polyvalency they lack in effective dose of any one constituent.

Elaborate studies of iron-deficiency anaemias have clearly shown the necessity for massive dosage of iron if a good result is to be obtained, and there are as yet no better iron preparations than iron and ammonium citrate, ferrous sulphate, or ferrous carbonate given in full dosage.

The adjuvant action of a full protein diet for blood production is often neglected. Protein is required for the formation of corpuscle stroma (globin) just as iron is necessary for the metallic constituent of haemoglobin. Extensive surveys of the incidence of iron-deficiency anaemias among the poorer and prolific classes (Heath and Patek, Davidson and Fullerton) have emphasized how near to a negative balance of iron intake are women during the period of reproductive life, and children at puberty. Foodstuffs rich in available iron and in proteins are necessary for the prevention of these mild but disabling anaemias. But, once established, these anaemias can be neither controlled nor cured by diet alone.

The most important fact to establish in an anaemia which is clearly due to iron deficiency is that haemorrhage is not a cause, because haematinic treatment is useless unless the bleeding is checked. When such is accomplished, the institution of Meulengracht's regime together with iron therapy considerably shortens the time required for blood regeneration.

Considerable improvements have been made in the treatment of pernicious anaemia and other macrocytic anaemias by the production of fractions of liver extract which are highly potent. Whereas many of these preparations, such as anahaemin, are effective in pernicious anaemia, and enable the maintenance dose for this disease to be reduced to as little as 2 c.cm. per month, there is much evidence (Wills, Clutterbuck, and Evans) that the highly purified products lack certain factors which are found in cruder extracts, and that the latter should be preferred for macrocytic anaemias other than pernicious anaemia, and indeed for pernicious anaemia itself, as a routine treatment in general practice.

It is now realized that blood transfusion has a useful place in the treatment of anaemias, but that the treatment is not without risk in a subject in whom the cardiac muscle has been rendered fatty by a long-standing anaemia. The administration of blood by the drip technique (Marriott and Kekwick) has obviated the danger of suddenly increasing the volume of circulating blood, has provided an ideal method for treating recurrent uncontrollable haemorrhage, has obviated the necessity for multiple small transfusions when these are not the treatment of choice, and has shown clearly that by con-

trolling an anaemia of toxic type, as in typhoid fever, it is sometimes possible to prevent a vicious circle of complications.

The treatment of the chronic type of anaemia known as splenic anaemia, or Banti's syndrome, has recently become much more conservative. It is now realized that splenectomy neither cures the disease nor reduces the liability to gastric haemorrhage. When splenectomy is performed, it is rational to perform at the same time some form of Talma-Morison operation for establishing a collateral circulation, and for relieving portal congestion. Operation should not be undertaken in patients with a high pre-operative platelet-count, as these are particularly liable to mesenteric thrombosis. Massive iron therapy is of value in the treatment of the anaemia of Banti's syndrome.

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CARDIOVASCULAR DISEASES

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The field of cardiology has widened in recent years, and several factors have contributed to this expansion. Foremost among these has been the introduction of improved methods of investigation connected with electrocardiography, radiocardioscopy, and to a lesser extent phonocardiography. Newer clinical syndromes relating to coronary disease, endocrine disorders, and pericardial affections have also been added, and surgery has demanded a trial in their treatment. Greater attention to peripheral arterial disease has expanded the horizon of the cardiologist, and the adoption of new medicinal remedies and the persistent enterprise of salesmanship enlisted on their behalf have made calls for assessment of their value based on controlled clinical trial.

An introspective analysis of the present position of cardiology with the object of prospecting its future course is best made by separate consideration of its different sections, under the four headings of clinical examination, special examination, medical treatment, and surgical treatment.

CLINICAL EXAMINATION

Blood pressure

The methods of measuring arterial blood pressure have been universally haphazard. There has also been general disagreement on the interpretation of findings obtained under identical conditions, particularly in regard to the point which designates the diastolic blood pressure. This diversity of views has its incidence alike amongst those who examine for life assurance and amongst other practitioners and even teachers of medicine. In effect, it is clear that writers discussing the several aspects of hypertension, especially its diagnosis, have often been at variance, largely due to the practice of different methods of measuring blood pressure, and partly because the findings have been subject to different interpretation. There has therefore been for some time a need for standardization of these methods, and, with the object of obtaining uniform and comparable blood pressure readings by all observers, a committee of British cardiologists has co-operated with a like committee in America and drawn up recommendations which will, it is hoped, receive general assent. Even when agreement is reached it will be necessary to know what constitutes a normal blood pressure at different ages, and, in order to set up this definition, cognizance should be taken of electrocardiographic and radiocardioscopic findings as well as those obtained from routine clinical examination, which will include a basal blood pressure reading taken under standard conditions. With regard to the electrocardiogram, the significance of inversion of the T wave in lead I together with deviation of the electrical axis to the left will need definition. Then, on radiocardioscopy, changes in the heart, notably left ventricular distension, may require a separate explanation from vascular changes in the form of elongation of the aorta.

Recent emotional disturbance or exertion will cause a temporary rise in blood pressure, and in the past a failure to appreciate this has led to erroneous

conclusions, and particularly to unnecessary rejection of applicants for life assurance. Thus it is a common experience in serial blood pressure readings to find the second and subsequent ones much lower than the first. The natural variation in the blood pressure has not been sufficiently recognized, so that unmerited praise has been apportioned in the past to certain medicinal agents used in the treatment of hypertension, and a natural decline in the blood pressure value has been mistaken for therapeutic hypotensive effects.

These several adjustments should ensure in the future a clearer conception of what constitutes pathological hypertension, and a better understanding of its response to natural and therapeutic stimuli.

Apex beat

The apex beat, designated as the lowest and outermost site of the cardiac impulse where the examining finger is uplifted, has assumed first importance in clinical examination of the heart, in that it provides the surest clinical index of the actual size of the heart. An outward shift of the apex beat, however, is as often a sign of cardiac displacement as of cardiac enlargement, so that before this physical sign is interpreted as evidence of left ventricular enlargement the common causes of displacement must be kept in mind, and excluded as operative factors. Thus the influence of tachycardia in dislodging the apex beat must be remembered before making a diagnosis of dilatation of the heart in a febrile illness. Again, thoracic scoliosis and a raised diaphragm from obesity or ascites commonly displace the heart outwards. Then the displacement of a non-distended left ventricle by enlargement of the right side of the heart in mitral stenosis and congenital heart disease will often cause difficulty in clinical diagnosis, and even radiocardiography in these instances fails to determine whether the left ventricle is enlarged or only displaced.

Percussion

Percussion as a means of detecting the size of the heart should be discarded as obsolete. It is inaccurate as a method of delineating the limits of even a grossly enlarged heart. The impression of cardiac enlargement gained from the finding of a displaced apex beat is always more precise than the evidence collected from percussion of the cardiac area. Adherence to this traditional method of examination of the heart can never advance our knowledge of cardiology, and it may produce harmful effects, in that it inevitably deceives both the teacher of clinical methods and his pupils. Even in the discovery of an aortic aneurysm dullness on percussion can seldom be a lone physical sign, for, when the vascular swelling has become so close to the chest wall as to give rise to dullness on percussion, its pulsation may be felt and seen. It cannot be denied that, when the pericardial sac has become distended with fluid, percussion will implement the clinical diagnosis, but even here the lesser degree of pericardial filling will only be disclosed by X-ray examination.

Murmurs

The interpretation of murmurs is changing as it acquires an anatomical or pathological basis in place of the physiological, which had a theoretical background. This change of view is largely the result of routine investigation by radiocardiography of patients presenting cardiac murmurs, and a keener scrutiny of the anatomical findings in those examined at necropsy. Phonocardiography, although now on trial, is not likely to add to our knowledge of the significance of murmurs.

The mechanism of mitral murmurs must come foremost under review. A newer conception of these accomplishes nothing unless it provides something

really helpful in clinical diagnosis and prognosis. With regard to the *pre-systolic* murmur, designating as it does mitral stenosis, it has been customary to refer to it as a diastolic murmur directly the rhythm changes from the normal to auricular fibrillation, although in quality it still remains rough, and in relation to several beats, especially if the rate is slow, it continues to be presystolic in time. In order to dispel argument on this trifling particular, is it not time we discarded the term 'presystolic' and referred to this murmur merely as 'diastolic', whether the rhythm is regular or not? In the meantime the recognition of a presystolic murmur establishes the diagnosis of mitral stenosis, so that, before applying to it this designation, due consideration must be given to it, bearing in mind that a loud and rough, or split, first sound may closely simulate the presystolic murmur of mitral stenosis. Such a sound is commonly present in conditions showing distension of the left ventricle, as in hypertension, aortic incompetence, and aortic stenosis, or again in lengthening of the P-R interval, bundle-branch block, and certain causes of tachycardia, notably thyroid toxæmia. Failure to distinguish these sounds frequently leads either to mistakes or controversy, the former illustrated by the erroneous diagnosis of mitral stenosis in cases only presenting hypertension, and the latter by the incitement of a debate on Austin Flint's murmur.

Concerning *diastolic* murmurs in the mitral area, there should be unanimity of opinion, in that they have only two causes, mitral stenosis and aortic incompetence. If the murmur is rough it usually indicates mitral stenosis, and if soft it establishes the presence of aortic incompetence.

Greatest lack of conformity, however, surrounds the question of the *systolic* mitral murmur, and agreement on its exact significance is not likely to be reached for some time. A few generalities are mentioned here which may help to substantiate certain truisms regarding it, and allot to this auscultatory sign a value in clinical diagnosis. In the first place, it might be regarded as a rule that, whenever a systolic murmur in the mitral area is taken to indicate disease of the mitral valve, it should carry the diagnosis of mitral stenosis and not of mitral incompetence, because in these cases it is the stenotic element that causes distortion in the outline of the heart leading to its dysfunction. In other conditions in which a systolic murmur in the mitral area is a conspicuous auscultatory sign, the sound most probably originates in the aortic valve or in a distended left ventricle and is unrelated to deformity of the mitral valve. Aortic stenosis, aortic incompetence, and hypertension are three disorders which commonly produce this murmur; if mitral *incompetence* were a feature in any of them it would be expected that the resultant regurgitation would lead to distension of the left auricle, but this eventuality does not arise, as is shown on radiocardiography and at necropsy. A recognition of this mechanism in producing the murmur should establish the precept that, in a patient of 50 years or over, a systolic murmur in the mitral area is more often evidence of left ventricular distension or of aortic disease than of mitral disease. Concerning a *late* systolic murmur, it may be said that if it is not an accompaniment of a distended left ventricle it can be regarded as a functional sound.

Adherent pericardium

Since the regular adoption of radiocardiography in the investigation of patients with heart disease, diagnosis of the lesion has become more precise, and workers in this branch of medicine have become aware of the infrequency with which they have diagnosed adherent pericardium. On rare occasions plaques of calcium compounds around the heart and puckering of the diaphragm visualized during X-ray examination have allocated the disease to the pericardium, and at the same time have given rise to a distrust of the signs which have been assembled for the clinical diagnosis of adherent

pericardium. Undulatory precordial pulsation, peri-apical systolic retraction, and retraction of rib spaces posteriorly are not pathognomonic signs of adherent pericardium. Cardiac enlargement almost never results from it. For these reasons it would be well if we gave little or no thought to the clinical diagnosis of this condition.

SPECIAL EXAMINATION

Electrocardiography

Although this can no longer be regarded as a new science, none the less within the last year or two so many valuable additions have been made in this branch of cardiology as to make it clear that this subject is by no means exhausted in providing newer aids in clinical diagnosis.

The introduction of chest leads is not likely to be revolutionary, nor is it expected to accomplish more than to provide the diagnosis of cardiac infarction in a few cases in which changes in the limb leads have not permitted this. Nevertheless, this aspect of the subject is engaging the attention of many workers, and more useful data may ensue. Lately, distinctive electrocardiograms have been described in connexion with right bundle-branch block, constrictive pericarditis, acute lesions of the pericardium, and pulmonary embolism; these findings have contributed in a valuable way not only to diagnosis but also to treatment.

Radiocardiography

Nowadays it hardly need be emphasized that an examination of the heart which does not include radioscopy is wholly inadequate. The argument that not all practitioners have access to an X-ray apparatus is untenable, because the fact remains that radiocardiography is invaluable in the confirmation of clinical diagnosis or its elaboration, in estimating prognosis, or in determining an unsuspected lesion. It is not intended here to dwell on the radiological findings of certain well recognized cardiovascular disorders, but merely to enumerate those conditions which will escape definition and even detection in the absence of radiocardiography. The following are some of the difficulties which this method of examination is capable of solving: the diagnosis of early aortitis; the more precise definition of congenital heart disease; the early recognition of heart failure; the diagnosis of hypertension when failure or infarction has lowered the blood pressure; the presence of constrictive pericarditis when this is suspected; early mitral stenosis, or localized aneurysmal dilatation of the descending aorta when the examination is aided by a barium-filled oesophagus.

Phonocardiography

It is improbable that this method of examination will ever become routine, and its use in the elucidation of murmurs is limited. Its main function in future is likely to be concerned with the interpretation of the third and fourth heart sounds whose presence initiates a triple rhythm on auscultation.

MEDICAL TREATMENT

Arrhythmia

Quinidine has now been in use for several years, but there is still no unanimity of opinion as to when it should be given. Too much has been written in the past about its contra-indications, and insufficient attention devoted to its indications. Like other newer remedies, quinidine has been prescribed indiscriminately in the treatment of diverse conditions, with the result that its therapeutic reputation is variable. The best results may be

expected from quinidine therapy in the following conditions: in those cases of thyrogenic auricular fibrillation in which the operation of subtotal thyroidectomy has failed to restore normal rhythm; in prolonged attacks of simple paroxysmal tachycardia even in the presence of heart failure; to annul premature beats when they become frequent and cause distress; in auricular flutter without failure; in other instances of auricular fibrillation in which heart failure symptoms and cardiac enlargement are absent, and when palpitation is troublesome.

Heart failure with auricular fibrillation

Two problems are presented by patients exhibiting abrupt heart failure with rapid auricular fibrillation, namely, the rapid induction of digitalis effect, and later the maintenance of efficient digitalization. On the Continent strophanthin has been preferred in the first circumstance, but in this country reliance has been placed in massive doses of some digitalis preparation. Recently a comparison of these several remedies was made in a series of patients, and digoxin proved to be most effective in bringing down quickly a rapid heart rate, although it was effective when given by mouth in a dose of 1.5 mg., it gave the best results when administered intravenously in a dosage of 1 mg.

For the maintenance of digitalization over long periods several digitalis preparations were given a controlled clinical trial in 18 patients with auricular fibrillation. Powdered digitalis leaf gave the best results, and this preparation, with the exception of the tincture, was also the cheapest remedy. Incidentally it was shown that coramine and cardiazol were without any beneficial effect in any of the cases, and the use of these two drugs in heart failure should be strongly opposed.

Heart failure with normal rhythm

The introduction of mercurial diuretics has completely changed the immediate prognosis in hypertensive heart disease manifesting failure; this form of therapy can quickly relieve the gross signs of heart failure, and, when prescribed occasionally and as a prophylactic measure, prevent their recurrence for long periods. Many such preparations are available, e.g. novurit and neptal, and may be given by the intravenous or intramuscular route, in the form of rectal suppositories, or even by mouth. The need at the moment is to find the best means of accentuating the diuresis produced by these preparations. It is likely that ammonium chloride or urea will prove to be the most efficient, but the best method of administering these is now on trial.

SURGICAL TREATMENT

Thyroidectomy

The treatment of thyrogenic heart disease and thyrogenic auricular fibrillation by subtotal thyroidectomy has become a routine procedure and reinstates normal rhythm in the majority of cases. Total thyroidectomy to improve intractable heart disease is still being evaluated, but its scope is likely to be limited; the operation, however, has established the precept that no patient with thyrogenic heart disease should be regarded as too ill to undergo surgical treatment. Thyroidectomy, although often capable of reducing the attacks of angina pectoris, is unlikely to produce results which will demand its routine adoption in the treatment of this condition.

Constrictive pericarditis

A temporary relief of ascites and oedema by the use of mercurial diuretics is all that can be expected from the medicinal treatment of this newer clinical syndrome, and surgical intervention in the form of partial pericardiectomy

should be given a trial, since it may occasionally produce great benefit from the unmasking of a constricted heart. The operation is often unsuccessful.

Hypertension

Inasmuch as medicinal treatment of hypertension has given such disappointing results it is natural that we should turn expectantly to surgery. Extensive removal of the splanchnic part of the sympathetic apparatus has produced lasting hypotensive effects, but sufficient time has not yet elapsed to allow us to judge of the value of this procedure in a large number of patients.

The initiation of a state of hypertension, by inducing renal ischaemia experimentally, and its relief, by removing the ischaemic kidney, has naturally directed attention to the finding of means of applying this procedure clinically. Already reno-omentopexy has been carried out in cases of hypertension with the object of relieving ischaemia, but so far without success. Even nephrectomy applied to an ischaemic kidney has been tried, but this method can only hold a promise of success in rare cases.

Ischaemia of limbs

To lessen the distressing symptom of claudication the application of intermittent venous occlusion is a simple physiotherapeutic method which often meets with considerable success. Surgery in the form of lumbar sympathectomy has occasionally given very satisfactory results, but only in those patients in whom a vaso-constrictor effect has been operative as demonstrated by 'temperature tests'. Unfortunately the common cause of ischaemia of the lower limbs is atherosclerosis, so that removal of the vasomotor control does not relieve the ischaemia. In a proportion of cases of thrombo-angiitis obliterans the operation gives satisfactory results. Ischaemia of the upper limbs is usually of Raynaud's type, and here the newer operation of cervical pre-ganglionectomy gives promise of good results without causing the distressing deformity associated with Horner's syndrome.

There is every indication therefore that the science of cardiology grows ever wider in its interests, and continues to make progress both in the diagnosis and treatment of diseases to which the heart and blood vessels are prone.

DERMATOLOGY

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THE BEGINNINGS OF MODERN DERMATOLOGY

Dermatology as a special study really commenced at the beginning of the last century. Although diseases of the skin had been known and described since the earliest times, and although a number of special works on the subject had appeared, it was not till Willan, with the collaboration of his co-worker Bateman, published his Atlas, in the opening years of the 19th century, that the classification of skin diseases was seriously attempted. Willan's classification was purely clinical, and was based on the appearance of the primary lesions.

During the century that followed hospitals and departments for the study of skin diseases appeared, the most notable being the St. Louis Hospital in Paris, which, in 1801, was converted into a dermatological hospital. Throughout the world individuals began to devote their time to the study of skin diseases. At first this study was mainly clinical, and the views of Willan and Bateman were modified and clarified by more careful study; but, simultaneously with this, a knowledge of the microscopic structure of the skin was gradually becoming acquired, and this enabled observers to correlate certain lesions with the anatomical structure of the skin.

Till the middle of the century little advance had been made in our knowledge of the aetiology of skin conditions; but, about this period, the older humoral theories began to be discredited, largely through the introduction of experimental methods by the Viennese dermatologist Hebra, and the importance of external factors in the production of skin lesions began to be realized. Later in the century came the development of bacteriology, and the importance of bacteria in cutaneous affections was quickly recognized. Fungous infection of the skin had been known since the middle of the century, but most of our knowledge of fungous diseases of the skin dates from the last two decades of the last century and is largely due to the work of Sabouraud.

During the present century, although the study of causative agents has still continued with a gradually widening field, more and more attention is being paid to the reactivity of the skin itself. This has been made possible by developments in the field of immunology. The advance of biochemistry is also rapidly opening up fresh fields for study in connexion with the dermatoses.

This is a very brief survey of the progress of dermatology during the last century and a half, and is a necessary preliminary to a discussion on the present position of dermatology.

PRESENT-DAY OUTLOOK IN DERMATOLOGY

One of the main changes in the outlook of dermatology to-day is that a large number of eruptions are no longer looked upon as specific diseases, but as

skin reactions. In other words, it is realized that a number of identical eruptions may be produced by a number of causes. The same is true to a lesser extent of the converse that the same cause may produce various lesions. Thus we have come to consider such conditions as eczema, urticaria, the erythemata, and the purpuras as group reactions rather than specific diseases, and these form the greater number of dermatoses met with in ordinary practice. There are, of course, some eruptions, for example psoriasis, which appear to be specific diseases and due to one cause, though the cause of this condition has not yet been demonstrated.

Eczema

It may be useful to consider the present position of the commonest of all dermatoses, eczema. Eczema is essentially a superficial eruption in which the epidermis and the papillary body (the vascular organ of the epidermis) are mainly involved. A number of clinical types are recognized, but they can be shown to be merely stages of the same condition. Formerly it was thought that eczema was a constitutional disease, but it was recognized even in Willan's time that irritants, both external and internal, played a part in the production of the lesions, and also that some individuals were more susceptible than others. Hebra was able to demonstrate that all the varieties of eczema could be produced experimentally by the application of irritants to the skin, and from his time onwards controversy as to the internal or external origin of eczema became acute.

An attempt was made to differentiate those cases in which eczematous eruptions were clearly produced by external irritants from cases in which such causation could not be demonstrated, reserving the term 'eczema' for the latter, and labelling the former 'dermatitis venenata'. There are some who still hold that there exists a type of 'idiopathic' eczema which is clinically distinguishable from eczematous eruptions produced by external irritants, but the majority of dermatologists to-day are not prepared to recognize such a clinical distinction.

The introduction of skin tests has not only added to the number of substances which are known to be capable of producing eczema in susceptible subjects, but has also enabled us to prove that certain substances were the cause of an eczematous eruption in particular individuals. It would appear, however, that something more than an irritant is necessary to produce an eczema; some abnormal sensitivity of the patient's skin has to be present. This sensitivity may be specific to certain definite irritants, such as we see in primula dermatitis, or the sensitivity may be more general, so that the skin reacts to a number of irritants. Specific sensitivity can be artificially induced, as has been shown by Cranston Low and others, but our knowledge of the causation of general sensitivity is still very meagre. It was at one time thought that various disorders of metabolism were responsible for eczema, and gout was particularly blamed. Biochemical research has not, however, confirmed this old view; indeed Bloch, writing in 1929, says that 'there is not the least evidence of the existence of a metabolic disturbance which is common to all or to many types of eczema pathognomonic for this condition of the skin. Viewed from the standpoint of physiological chemistry, eczema is not a metabolic disease.'

An interesting feature of eczema is the tendency for lesions to come out in varying parts of the body. A single patch may be produced in a sensitive skin by any local irritant, as one so frequently sees in trade eczemas, but, after the original irritant has been removed, patches may appear in other places. This dissemination of eczema has naturally led to the suggestion of some constitutional disturbance, but opinion is now turning to the idea of the production of toxic chemical substances in the primary patch which, when circulating in the blood stream, may produce lesions of a similar type at

distant sites. Some years ago Whitfield showed that skin eruptions might develop during the absorption of subcutaneous haemorrhages. Possibly the production of the original patch is due to the development in the skin of toxic chemical products in the first instance.

Urticaria

This certainly appears to be the case in urticaria, in which Lewis has demonstrated the presence of a histamine-like substance which appears to be responsible for the production of the wheal. This substance can apparently be released in the tissues by a number of different irritants, some externally applied, such as heat and cold, or trauma, or more commonly by the absorption of toxic substances into the blood stream. More recently Grant has suggested that in cases of urticaria due to nervous influences, acetylcholine may be released into the tissues and may cause the urticarial reaction. Urticaria has long been recognized as a reaction of the skin to a number of toxins, foodstuffs, drugs, vaccines, and sera, as well as possibly to bacterial toxins, which are capable of eliciting such a reaction in a sensitized skin.

Erythematata and purpuras

The erythematata and certain purpuras also appear to be reactions of a similar type, though usually excited directly by bacteria or their toxins. Erythema nodosum is an interesting example of this. Formerly thought to be a specific reaction, and often grouped among the rheumatic diseases, it is now recognized that certain cases are tuberculous in origin. Though some observers would say that all cases of erythema nodosum are tuberculous, this view is not accepted by most dermatologists, who consider that this condition is a skin reaction which may be evoked by more than one organism.

Tuberculosis

It will thus be seen that the dermatologist has to deal with a large number of skin conditions each of which may be induced by a number of causes. We may now consider how one toxic agent may produce various skin lesions. Syphilis and tuberculosis are good examples. In tuberculosis we see examples of localized involvement in the form of lupus vulgaris, verruca necrogenica, and the tuberculous chancre; of secondary involvement from infection of deeper structures, as in scrofuloderma; and of dissemination by the blood stream, as in the tuberculides. Tuberculosis has also been considered responsible for a number of other conditions, such as lupus erythematosus and sarcoidosis; of this, however, proof is still lacking.

Fungous infections

Our knowledge of fungous infection of the skin has increased very considerably during recent years. Though ringworm of the scalp, which was very prevalent during the earlier years of the present century, has considerably diminished, the demonstration by Whitfield, in 1910, of ringworm fungus in intertriginous conditions between the toes, and subsequent work on the subject, have shown that certain forms of this infection, previously unrecognized, are extremely prevalent. More recently, infections of the skin by monilia—organisms allied to that of 'thrush'—have been demonstrated. Ringworm of the toes and of the groins (dhotie itch) has become so prevalent, especially in institutions where numbers of youths and adolescents are collected, that the epidemiological problem has become acute. In connexion with fungous infections, Jadassohn has shown that generalized eruptions can be produced by absorption of toxins into the blood stream, producing lesions analogous to the tuberculides.

RELATION OF DERMATOLOGY TO GENERAL MEDICINE

Turning now to a consideration of the relationship of dermatology to general medicine, it would seem that modern research in dermatology has tended to show that the skin is a rather self-contained organ, and that the majority of skin conditions seen in ordinary dermatological clinics are not associated with general manifestations. There are, of course, many general infections which affect most organs of the body, the skin included, such as the acute specific fevers and syphilis. In tuberculosis, however, when the skin is affected other organs, apart from the lymphatic system, are frequently free from obvious infection. Fungous disease rarely produces visceral involvement. Eczema seems rarely to be associated with any general disease, and patients with eczema are generally otherwise well. As pointed out on page 63, it has been impossible up to the present to point to any definite disturbance of metabolism specially associated with this condition. Gout was at one time looked upon as a potent cause of eczema, but, in spite of the decreased incidence of gout, eczema shows no abatement.

Rheumatic diseases

The connexion between the skin and the rheumatic diseases, once thought to be so common, is not at all clear to-day. Joint pains and swelling occasionally accompany certain urticarias and erythemata, but the association between true articular rheumatism and skin lesions is very indefinite. There is, however, a very definite association between psoriasis and one type of rheumatoid arthritis, though cases of this kind are not common.

Metabolic conditions

Certain definite metabolic diseases of the skin, such as xanthoma, are recognized as being associated with disturbance of fat metabolism, and certain rare conditions as being associated with disorders of protein metabolism, while in diabetes some tendency to local eczema exists, and a special sensitiveness to infection by pyogenic organisms appears to be present. In certain conditions involving the blood-forming organs, such as leukaemia and lymphadenoma, pruritus, erythrodermia, and skin tumours occur.

Endocrine disorders

Certain conditions of the skin occur in disorders of the endocrine glands, as for example the peculiar skin in myxoedema, which may also occur in a localized form in toxic goitre. The pigmentary changes in Addison's disease are well known, and various disturbances of hair growth are found in adrenal cortical hyperplasia. Acromegaly and cutis verticis gyrata are associated with pituitary disease. Some relation exists between the development of the sex glands at puberty and acne vulgaris, though the whole mechanism of the process is not yet clear.

Diet

Much work has been done in recent years in the attempt to elucidate the relationship of diet with skin disease, but without very definite results. Vitamin deficiency is responsible for at least two well-defined conditions, scurvy and pellagra, and others less definite have also been described.

Psychological factors

The psychological factor in skin diseases is of great importance and is being carefully studied, and in this field we may hope for fruitful study in the future, though at present views are rather conflicting.

It may be that the impression has been conveyed that skin diseases can to a large extent be dealt with without much attention to the patient's general

health. This is far from being the case. Though the direct relationship of skin diseases to well-defined general diseases is not often clear, yet for the successful treatment of skin conditions the general and mental treatment of the patient is all-important.

The future of dermatology as a science seems to be bound up with the development of biochemistry. Most of the immunological studies which at present are occupying the attention of research workers can only be solved on chemical lines. No doubt new clinical conditions will continually be separated from more composite groups, and further knowledge is still to be obtained in bacteriology, particularly in relation to virus diseases, but it may be that some conditions in which we have looked in vain for some bacterial cause may in the long run prove to be due to autogenous chemical toxins.

PROTAMINE INSULINS IN DIABETES MELLITUS

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The introduction of protamine insulin by Hagedorn in 1935, and its modification by Scott into zinc protamine insulin in the following year, together constitute the greatest advance in the treatment of diabetes mellitus since the discovery of insulin.

Many efforts had previously been made to prolong the action of insulin, but it was not until Hagedorn and his co-workers in Copenhagen carried out a series of experiments on the solubility of insulin combined with different protamines that any real progress in this direction was made. The outcome of these experiments was the production of a protamine insulin suspension which was found, when injected subcutaneously, to be absorbed considerably more slowly than soluble insulin hydrochloride, and to possess a more prolonged hypoglycaemic action; this substance was termed protamine insulin.

In 1936 Scott and Fisher, acting on the results of experiments on the zinc content of insulin preparations, tried the effect of adding small quantities of zinc to protamine insulin, and thereby produced a new compound, zinc protamine insulin, the hypoglycaemic action of which was found to be even more prolonged than that of protamine insulin.

CHEMICAL COMPOSITION AND PHYSIOLOGICAL ACTION

The protamines are elementary compounds of amino-acids containing one or more of the basic constituents lysine, arginine, and histidine, and are obtained from the ripe sperm of fishes. In the preparation of protamine insulin a monoproamine derived from *Salmo iridius* is used on account of its minimal solubility being at pH 7.3, that is, near the reaction of serum. This substance forms a fairly stable and relatively insoluble compound with insulin.

Two such compounds are now manufactured which differ in certain important particulars.

Protamine insulin

(*Synonyms*.—Danish protamine insulin; protamine insulinate; Retard insulin)

In order to prepare this type of insulin for injection it is necessary to add 1 c.cm. of a buffer solution containing sodium phosphate to 5 c.cm. of an acid solution of protamine and insulin, the resulting cloudy suspension being shaken before each withdrawal. The suspension so formed can now be prepared in two concentrations according to the strength of soluble insulin used, namely, 40 or 80 units per c.cm., and must not be kept for more than four weeks.

Zinc protamine insulin

[*Synonyms*.—Protamine zinc insulin; Canadian protamine insulin; protamine insulin (with zinc) suspension]

Scott and Fisher found that the addition of traces of zinc to protamine insulin and the adjustment of the pH to 7·2 resulted in the production of a zinc protamine insulin compound more stable and more prolonged in action than any previously discovered. This compound is supplied as a suspension in concentrations of 40 and 80 units per c.cm., keeps well and, after shaking, is ready for immediate use. As only 1 mg. of zinc is added to 500 units of insulin, it is unlikely that the zinc will produce any ill effects even after long continued use.

The physiological actions of protamine insulin and of zinc protamine insulin have been summarized and compared with that of soluble insulin by Lawrence in the following table:

TYPE OF INSULIN	IN DOSES	DURATION OF ACTION	COMMONEST TIME OF HYPOGLYC.	REMARKS ON TYPE OF ACTION
Soluble	to 10 units	5-6 hours	2-4 hours	Quick and strong. Balances much carbohydrate
	to 20 "	6-8 "	3-5 "	
	to 40 "	10-12 with big doses	6-8 "	
Retard (protamine insulin)	to 20 units	8-10 hours	4-6 hours	Slower. Balances less carbohydrate
	to 40 "	12-16 "	6-9 "	
	to 60 "	Occasionally 24 hours	7-12 "	
Zinc-protamine-insulin	to 10 units	6-8 hours	5 hours	Very slow. Balances carbohydrate poorly
	to 20 "	to 12 "	8-12 "	
	to 30 "	to 18-24 hours	8-20 "	
	40 units or more	24 hours or longer	16-24 "	

From the above table it will be observed (i) that the duration of action in each type of insulin depends upon the amount injected, and consequently that the commonest time of onset of hypoglycaemia varies not only according to the type but also the dosage of insulin used; and (ii) that zinc protamine insulin is the only preparation which in moderate doses acts for twenty-four hours or longer.

THERAPEUTIC USE OF PROTAMINE INSULIN PREPARATIONS IN DIABETES MELLITUS

For practical purposes it is convenient to accept the hypothesis put forward by Lawrence that in a normal person the pancreas produces a continuous supply of insulin which controls endogenous carbohydrate metabolism, and that this is supplemented by the secretion of larger amounts of insulin in response to the stimulus of ingested carbohydrate. If this view is correct, it is clear that, in order to attain anything approaching physiological perfection in the control of diabetes mellitus, an insulin preparation is required which combines a prolonged and steady hypoglycaemic action with ability to act strongly and rapidly in response to the hyperglycaemia induced by carbohydrate food.

At the present time this twofold action cannot be obtained by the use of any single insulin preparation, but it is to some extent represented by the combined actions of the protamine insulin suspensions and soluble insulin. This being so, it is easy to appreciate the great advance in the treatment of diabetes mellitus effected by the introduction of these new insulins both in reducing the number of injections required and in providing a relatively

simple method of obtaining a better control of the blood-sugar level throughout the twenty-four hours.

Protamine insulin (referred to below as Retard)

The advantages of Retard over soluble insulin are its more prolonged action and diminished tendency to produce hypoglycaemic attacks; the disadvantages are its weaker action on ingested carbohydrate, less regular absorption, and the fact that, when it does produce hypoglycaemia, the attacks may be insidious in onset, variable in relation to the time of injection, and severe. These properties led Krarup and other early workers to use protamine insulin for the evening injection and ordinary insulin in the morning. In this way it was found possible in severe cases to control the blood-sugar and abolish ketosis during the night without serious risk of producing hypoglycaemia, and also reduce the morning requirement of soluble insulin by keeping the fasting blood-sugar at a lower level.

Retard may also be used for both morning and evening injections in insulin sensitive cases in which soluble insulin tends to produce wide fluctuations in blood-sugar and consequently frequent attacks of hypoglycaemia. Hitherto such cases required multiple injections of insulin but, by giving Retard in the morning, it is possible both to reduce the number of injections and diminish the risk of hypoglycaemia. This method only succeeds, however, in relatively mild cases, more severe cases requiring the addition of soluble insulin in the morning if heavy glycosuria during the day-time is to be avoided. According to Graham the addition of soluble insulin to both morning and evening doses constitutes the best method of controlling very difficult cases but has the disadvantage of being somewhat complicated. Mild cases on two small doses of soluble insulin can often be controlled by one morning injection of Retard about equal in amount to the combined doses of soluble insulin, but zinc protamine insulin, by virtue of its longer action, is at present the ideal preparation for use in such cases. (See below.)

Protamine insulin is not greatly used now in this country or America, its place having been taken to a large extent by zinc protamine insulin.

Zinc protamine insulin (referred to below as Z.P.I.)

This is the ideal insulin to use in mild cases of diabetes mellitus in which restriction of carbohydrate intake to between 100 and 150 grams a day alone fails to control the hyperglycaemia and glycosuria. These patients are often, but not always, elderly, and one injection of Z.P.I. in the morning before breakfast usually controls the diabetes satisfactorily. The amount varies in different cases, but the following simple scheme enables the correct dose to be arrived at with the minimum of pathological investigations, and little risk of hypoglycaemia.

The patient is put on a diet containing, say, 120 grams of carbohydrate which should be distributed fairly evenly throughout the day in the following manner:

Breakfast	—	—	—	30	grams C.
Lunch	—	—	—	30	„ C.
Tea	—	—	—	20	„ C.
Dinner	—	—	—	30	„ C.
Bed-time	—	—	—	10	„ C.

All patients receiving Z.P.I. should be given 10 to 20 grams at bed-time as a precaution against nocturnal hypoglycaemia. An initial dose of 16 to 20 units of Z.P.I. is given about half-an-hour before breakfast, and samples of urine are tested for sugar before meals and at bed-time; these specimens are almost sure to contain sugar on the first day unless the patient is abnormally sensitive to Z.P.I. Next morning the same dose is repeated, and specimens

are tested on rising, and immediately before breakfast, as well as at the other times indicated. It is important to test two specimens before breakfast as the first may contain sugar as a result of a rise in blood-sugar following the bed-time feed, and is therefore a less reliable guide to the fasting blood-sugar than the second. It is unwise to change the dose of Z.P.I. for the first few days, unless the second morning specimen is sugar-free on two consecutive days; in such a case it should be lowered by four units to avoid the risk of hypoglycaemia, the action of Z.P.I. during the first few days being cumulative. If the second morning specimen continues to contain more than a trace of sugar, the dose should be increased by 4 units every third day until it is sugar-free, or almost so, it has been found that, if this specimen is completely free of sugar for three consecutive days, there is a considerable danger that the patient may become hypoglycaemic in the night or early morning, and the dose should be reduced by 4 units.

If this routine is carried out, most mild cases pass little or no sugar, except possibly immediately after meals, ketosis disappears, and there is marked improvement in weight and general health.

EXAMPLE 1

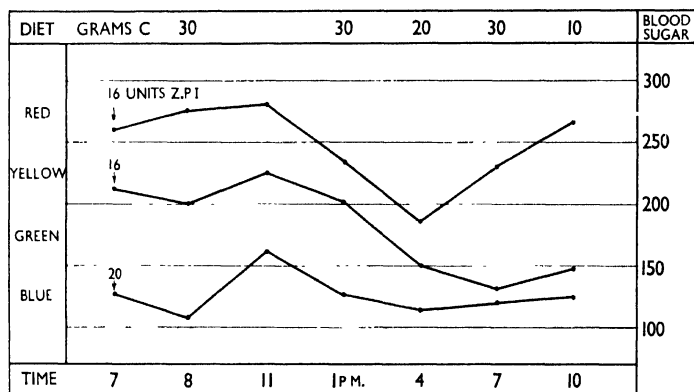


FIG. 1—Curves taken on 1st, 4th, and 7th days. Intermediate days not shown.
Colours represent results of Benedict test for sugar in urine

This method of treatment fails in severe cases of diabetes mellitus because Z.P.I. is unable to control the hyperglycaemia induced by ingested carbohydrate. Any attempt to keep the urine sugar-free during the day-time by one morning dose of Z.P.I. is almost certain to fail, or cause hypoglycaemia in the late afternoon or night; this can only be avoided by using a smaller dose of Z.P.I. together with sufficient soluble insulin to control the glycosuria by day.

Zinc protamine plus soluble insulin

If the principles laid down for the use of one dose of Z.P.I. are combined with those already well known for the use of soluble insulin, this method of control should present little difficulty. To give a mixed injection, air is first injected into the bottle containing Z.P.I.; the needle is then transferred to the bottle of regular insulin and the correct dose drawn into the syringe; the needle is then reintroduced into the Z.P.I. bottle and the requisite dose withdrawn.

As patients requiring a mixed dose are usually younger, a higher calorie diet is required, and the greatest concentration of carbohydrate should be in the earlier part of the day, for example:

Breakfast	-	-	-	50	grams C.
11 a.m.	-	-	-	10	" C.
Lunch	-	-	-	40	" C.
Tea	-	-	-	20	" C.
Supper	-	-	-	30	" C.
Bed-time	-	-	-	10	" C.

Unless there is severe ketosis the best way to start treating a case by one mixed injection is to find the dose of Z.P.I. which will render the second morning specimen completely or almost sugar-free. When this is done about 8 to 20 units of regular insulin, according to the severity of the case, are added, and the dose is increased or decreased until the blood-sugar immediately before the mid-day meal is between 100 and 140 mg. per cent. If blood-sugar estimations are not available, some idea of the correct dose of regular insulin may be obtained by testing the specimen passed immediately after lunch, the bladder having been emptied just before lunch, but it is much better to estimate the blood-sugar.

As the fasting blood-sugar is likely to be low when Z.P.I. is being used, the mixed injection should be given immediately, instead of half-an-hour before breakfast, in order to avoid the danger of hypoglycaemia being produced by the soluble insulin before food is taken.

While most moderately severe, and even severe, diabetics can be satisfactorily treated by a single mixed dose in this way, there remains a small number of patients in whom treatment by this method results in heavy glycosuria and ketosis towards the end of the day when the regular insulin has ceased to act and the Z.P.I. alone is acting too weakly to control the hyperglycaemia. In these cases it is best to give a small evening injection of soluble insulin, either before tea or dinner, the former being preferable as it allows the soluble insulin more time to complete its action before the patient goes to bed and, being followed by two meals instead of one, offers less risk of the occurrence of hypoglycaemia during the night.

EXAMPLE 2

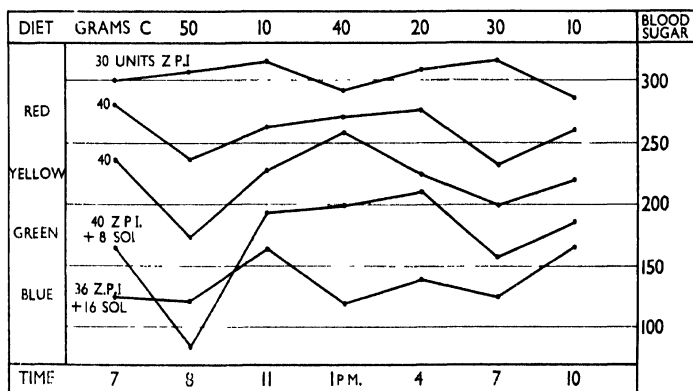


FIG. 2.—Curves taken on 1st, 4th, 7th, 8th, and 12th days. Intermediate days not shown. Urine tests as in Example 1. *N.B.* On the 8th day the blood-sugar at 8 a.m. was too low, and the dose of Z.P.I. had to be reduced by 4 units

THE CHANGE FROM SOLUBLE TO PROTAMINE INSULIN

In order to change over from two doses of soluble to one dose of Z.P.I. the severity of the case must be considered. In mild cases taking up to 20 units of soluble insulin a day it is safe to give an equal dose of Z.P.I. and adjust by the addition or subtraction of 4 units as already described.

In more severe cases it is advisable to treat the patient in a hospital or nursing home, as it is essential to avoid a severe relapse of the diabetes. To assess the correct dosage is largely a matter of trial and experience, but it is safe to start with a dose of soluble insulin slightly smaller than that usually taken in the morning together with a slightly larger dose of Z.P.I. but not more than 40 units; it is important to give a bed-time feed in all cases.

It is often difficult to decide whether to change over from two doses of soluble insulin to one mixed dose but, as a general rule, cases which are well balanced and contented on two doses are better left alone, as are also those whose life is irregular in respect to meal times and exercise.

HYPOGLYCAEMIA

The symptoms and signs of hypoglycaemia following the use of protamine insulin preparations are similar in most respects to those produced by soluble insulin, but tend to be milder, slower in onset, and less obvious to the patient; they may, however, be equally severe and more prolonged. The commonest time of onset is given in the table on page 68, and varies according to the type of preparation and dosage used. Morning headaches relieved by breakfast, nausea, and drowsiness are common symptoms of hypoglycaemia due to Z.P.I. and, since these are uncommon after soluble insulin, they are liable to pass unrecognized, with serious consequences.

As the blood-sugar may reach a very low level before hypoglycaemia is recognizable, it is important in treatment to give plenty of sugar not only to effect a rapid relief of symptoms but also to prevent their recurrence, which is otherwise not uncommon.

CHILDREN

The protamine insulins have proved of great value in the treatment of juvenile and infant diabetics. The difficulty in controlling diabetes mellitus in children without producing hypoglycaemia is well known, and the use of multiple injections is particularly to be avoided. With the aid of Z.P.I. or Retard it is usually possible to avoid the wide fluctuations in blood-sugar produced by soluble insulin and, what is even more important, to abolish ketosis and reduce the incidence of hypoglycaemic attacks. The method of use does not differ in principle from that already described for adults, but in infants considerably smaller doses should be given; it is often possible, for example, to control diabetes in infancy with one dose of from 6 to 12 units of Z.P.I. without the addition of soluble insulin.

OPERATIONS AND EMERGENCIES

Although the protamine insulins may be useful in experienced hands to act as a background to treatment with soluble insulin, it is probably better in our present state of knowledge to rely on the quick-acting soluble insulin in diabetic coma and other emergencies.

CONCLUSION

The protamine insulins have not displaced soluble insulin in the treatment of diabetes mellitus, but have added considerably to the efficiency with which

this disease can be treated, and have also helped to remove some of the limitations and inconveniences attendant upon the older methods.

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THE EXANTHEMATA AND DIPHTHERIA

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The present century has witnessed a considerable and almost uniformly progressive decline in mortality from the acute infective diseases and, with the notable exception of typhoid fever, this has been accompanied by a similar, but not always parallel, fall in case-fatality. It is only natural that therapeutists should ascribe the improved chances of recovery of their patients to more highly specific or, at least, more rational treatment, but such bacteriological and epidemiological data as are available should provide a warning against a too facile acquiescence in this view. For example, a decline in the severity of scarlet fever and smallpox is generally conceded but the question of reduction in the severity of closely allied streptococcal infections or of measles is rarely seriously entertained. Nevertheless, evidence is accumulating that certain factors, probably complex in their character and fluctuating in their influence at different times, have determined the intensity of toxic-infective processes in the past and will probably determine the future trend of epidemiological happenings. What these factors are, the conditions which govern them and which they in their turn govern, and their effect on the individual and the herd, concern alike the clinician, the sanitary administrator, and the epidemiologist. Some of these factors are considered *seriatim* below.

FACTORS WHICH DETERMINE THE OCCURRENCE OF ACUTE INFECTIVE DISEASES

Specific immunity

The most important factor is the specific immunity level of the population at risk; numerous examples are available of malignant forms of infective diseases, as in smallpox, diphtheria, and typhoid fever, being completely eliminated by mass immunization of those communities among which they once flourished in epidemic form and in all probability would reappear should vigilance be relaxed.

But, as the menace of a particular disease recedes either by reason of its rarity or its lowered lethality, the individual becomes more reluctant to submit to the inconvenience or risk inherent in the measures employed for its prevention. The crucial time may come, as it has come in respect of smallpox, when even the most enthusiastic immunologist may pause to consider if the measure is really necessary in view of the negligible risk of attack. For some diseases, and in certain circumstances for all diseases, short-term immunity is more practicable as an emergency measure, and is usually conferred by introducing pre-formed antibodies into the circulation, commonly by the parenteral route.

Multiplication, dissemination, and destruction of the *materies morbi*

The simplest solution of the control and final abolition of the infective diseases would be complete destruction of the infecting agents, or at least

their inhibition, and restriction of their range of activity. The chief obstacle to this method, even if it were capable of execution, is the difficulty of applying it over a sufficiently wide area, and the great risk involved should the diseases in question be subsequently reintroduced to a completely susceptible community, as happened in the Fijian Islands in respect of measles. Nor does experience give any support to the hypothesis that the micro-organisms of disease would die out owing to lack of suitable hosts; on the contrary, to give a common example, carriers of diphtheria organisms have sometimes been observed to increase in prevalence in a community following immunization of the susceptibles. Nevertheless, no attempt made to check the activities of micro-organisms, sporadic cases of disease would often, although not inevitably, lead to minor outbreaks, and outbreaks to epidemics.

Segregation of cases and contacts

The isolation of cases and carriers in hospitals or in the home has failed to effect an appreciable reduction in the incidence of the acute infective diseases, and fever hospitals are now regarded as centres for treatment rather than as asylums for the segregation of the infective from the healthy, for which they were originally designed. Although it is still the current practice to treat the more deadly diseases in hospital, the segregation of contacts has been largely replaced by a system of supervision and daily inspection, if required, for the earliest manifestations of disease, this change of policy has not resulted in any increase in the incidence of disease, and the expense entailed by loss of education and provision of isolation accommodation is avoided. Nevertheless, some control over contacts and proved carriers is necessary; in this connexion instruction in the elementary rules of hygiene and restriction in dealing with food usually suffice as far as the enteric-dysentery diseases are concerned, although every attempt at elimination of the infecting agents should continue. Carriers of respiratory infections provide a more serious problem, as curative measures often prove unavailing, and it may be difficult to limit their potential range of infectivity without curtailment of personal liberty or considerable economic loss. In the recent epidemic of acute poliomyelitis in the United States and Australia, and to a less extent in certain areas in this country in 1938, the best single measure in checking the spread of the disease was held to be isolation of immediate contacts and restriction of travelling from infected to healthy zones. The speed of modern travel, whereby long distances are covered in a shorter space of time than the majority of incubatory periods, has introduced a new element of danger and may demand a period of quarantine for new arrivals, at least from an infected area.

Nutritional and environmental influences

Other possible factors must be considered, which may influence morbidity and, perhaps to a greater degree, fatality. The recent improvement in the general standard of nutrition and personal hygiene, and of housing and education, is partly the cause and partly the result of the fall in the birth-rate; in connexion with this there has been a demonstrable shift in the age incidence of the common infective diseases of children from the pre-school age group to the higher age groups, the individuals composing which are in every way better prepared to withstand toxic-infective processes generally. In a recent statistical study (Cheeseman, Martin, and Russell) this trend was clearly shown to have occurred in respect of diphtheria and was ascribed to the social and economic circumstances which determine in some measure a decline in the birthrate, rather than to a hypothetical alteration in the virulence of *C. diphtheriae*. Inadequate or inappropriate nutrition, accompanied by iron and vitamin deficiency, was probably an important factor in initiating, at least, the influenza pandemic of 1918; once the disease acquired epidemic character, perhaps due in part to exaltation of the virulence of the virus,

countries only indirectly affected by the war were successively involved. In like manner, the emergence of a malignant form of scarlet fever in south-eastern European countries in the years immediately following the war of 1914-18 was mainly due to the unfavourable social and economic conditions of the peoples concerned; at least, by ordinary bacteriological tests little alteration could be detected in the virulence of the causal organisms compared with strains isolated at the same time in this country. Limitation of the size of families with or without a rise in the standard of living is likely to result in a fall in the immunity level of the population, owing to diminished chances of exposure and its corollary, latent immunization, and the necessity of seeking protection by artificial means is therefore correspondingly increased. Certain technical difficulties in connexion with the preparation of potent and safe antigens must be overcome and a fuller knowledge gained of the conditions of administration requisite for complete success before the conquest of the infective diseases by specific prophylaxis alone can be regarded as practicable.

SPECIFIC PROPHYLAXIS

Enteric fevers

In countries where sanitation is sound, specific immunization against the enteric fevers is unnecessary under normal conditions, but accidents may occur occasionally despite every precaution. For a limited number of persons intimately exposed, passive immunization by means of Felix's Vi antiserum, 20 to 30 c.cm. given intramuscularly as soon as possible after exposure, is a rational procedure and may afford protection for 14 to 21 days; should the risk of infection continue this may be followed up by 2 or 3 inoculations of antityphoid vaccine at 7 to 10 days' interval. The possibility that inadvertent administration of vaccine in the early stages of invasion by the disease may lead to a severe reaction, so-called 'provocation typhoid fever', must be faced, but its occurrence is too infrequent to be considered seriously as a contra-indication.

The severity of the reactions which may follow prophylactic inoculation of vaccines has directed attention to modifications of the customary suspensions of killed organisms. Recently an endotoxoid (Grasset) prepared from typhoid strains with Vi antigen, containing higher immunizing properties and causing less reactions than ordinary or detoxified vaccines, has been tried with considerable success under field conditions amongst native workers in South African gold-mines. An alum-precipitated modification, similar in principle to that for diphtheria, has also been shown by the same worker to produce a high agglutination titre which has lasted for a year or longer. The parenteral route appears to be essential to yield the best results; oral administration of vaccines is unattended by untoward reactions, but the immunity conferred is characteristically transient and uncertain.

Diphtheria

During the last few years evidence has been accumulating that the conventional Schick-test level of $\frac{1}{10}$ unit of antitoxin per c.cm. of blood may not provide complete security from invasion by highly virulent (usually starch-fermenting) strains of *C. diphtheriae*. In the absence of direct titration of the blood antitoxin, an impracticable procedure for routine use, it may be advisable in special circumstances, e.g. if malignant diphtheria is prevalent, to give periodical single injections of antigen at intervals even to Schick negative reactors. The choice of the antigen should vary according to the sensitiveness of the individual; for all children and the majority of adults, formol toxoid (three inoculations at intervals of 2 to 3 weeks) is suitable, causing few reactions and possessing high immunizing properties, but for highly sensitized subjects (Schick pseudo-positive and Moloney positive reactors), usually adults

who have already undergone invasion—manifest or latent—toxoid-antitoxin floccules are preferable. The early hopes that one injection of alum-precipitated toxoid would suffice to confer complete and lasting immunity have not generally been fulfilled; the current practice is therefore to give two injections at an interval of 2 to 3 weeks or longer, and to repeat the Schick test 4 to 6 months after the last injection. Because of the risk that the second injection may provoke a violent reaction in hypersensitive subjects, Jensen recommended and used with considerable success the nasal instillation of antigen to complete the process of immunization initiated by a single subcutaneous dose, or to restore a lapsed immunity. The method has not yet been adopted on any scale in Great Britain.

Scarlet fever

So prone are non-immunes to severe allergic reactions or to attacks of 'miniature scarlet fever' after inoculation of a potent Dick toxin, and so inconstant and, in many instances, so evanescent is the immunity produced even by a full course of 5 inoculations (commonly comprising 80,000 skin test doses in all), that many workers have abandoned the measure as not being worth while. Experiments with detoxified preparations (formol toxoid) have not been uniformly successful; some of the earlier toxoids gave rise to more violent reactions than raw toxin, and specially purified and concentrated toxins have not proved more satisfactory on clinical trial. The method has been found of value in the protection of subjects specially exposed to risk, such as nurses in fever hospitals in whom the success usually achieved is due in large part to the constant antigenic stimulus they receive from close contact with cases of scarlet fever, and in closed or semi-closed communities, such as residential schools and orphanages, to which fresh batches of susceptibles are admitted from time to time and tend to add fresh fuel to the epidemic fires. Under suitable conditions, antibacterial immunity may be added to antitoxic immunity, with consequent diminished liability to streptococcal tonsillar and pharyngeal affections. Passive immunization by means of immune serum has been shown to have only a limited scope in prophylaxis, transient in action, 10 to 14 days at most, it is prone to induce horse serum allergy, although the latest preparations of sera ('globulin modified' by elimination of albumins and partial digestion of the globulins) cause but trivial and infrequent reactions.

Measles

Temporary protection or mitigation of the character of attack may readily be secured for individual contacts or groups of contacts by timely administration of measles immune serum, provided that the fact of exposure is known with certainty. Exposure, whether accidental or deliberate, must be intimate in order to be effective, and there is no ready means of determining its effectiveness in a given case; certain observations, such as Goodall's 'illness of infection', leucopenia, or loss of weight in the incubatory stage, may sometimes provide a clue although singly they are not constant enough to merit reliance. A recently reported attempt (Lempriere) to apply serum prophylaxis to the personnel of a large public school was only partially successful and illustrates well the apparent vagaries of exposure and infection, which are largely beyond our knowledge and control. The difficulties inherent in the method are increased by the lack of a ready means of determining the protective potency of the reagent, apart from observation of its results on clinical trial. Convalescent serum has shown itself to be more than twice as potent, volume for volume, as adult serum, and is the only reliable means for vouchsafing protection; placental extracts occupy a place approximately intermediate between convalescent and adult serum, depending on the method of preparation and the degree of concentration attained. Sera prepared from different animals, horse,

goat, or sheep, by inoculation of organisms or of patients' nasopharyngeal washings in which the presence of living virus is assumed, have not proved to be effective and have been abandoned generally. Serum tends to show indications of deterioration after 9 to 12 months even although stored under proper conditions at 4° C. By drying fresh serum to powder form potency can be maintained unimpaired probably indefinitely, but sufficient time has not yet elapsed for adequate observations to be made on its longevity.

Whooping-cough

It is now generally admitted that the early failures to confer immunity against whooping-cough were due to the use of old stock 'rough' cultures which were antigenically inert. The latest studies (Lawson; Kendrick and Eldering) suggest that suspensions of freshly isolated strains in the 'smooth' antigenic phase are preferable as antigens to detoxified vaccines or endotoxin extracts. From 3 to 5 inoculations of gradually increasing doses are given at half-weekly to weekly intervals, the total dosage being usually some 80,000 million organisms. The immunological response to the injections may be estimated by means of the complement fixation test; absent or weakly positive reactions suggest the need for further injections until a maximal response is obtained. As immunity from inoculations tends to be short-lived, an abbreviated course (1 to 3 injections) may be given some weeks in advance of an expected epidemic, until the age of 6 to 7 years, when the disease is rarely other than trivial in healthy subjects. Immunization should begin as early as the sixth month or even earlier if there is special risk of exposure, but if the child lives a sheltered existence it may be deferred until school age is approached. Contacts may be inoculated in the incubatory period or in the catarrhal and early paroxysmal stages with a reasonable prospect that some measure of mitigation of attack may be afforded. Convalescent serum has not found a place either in prevention or in attenuation, partly because of the difficulties of obtaining supplies of serum, and partly because the disease is not highly infective under ordinary conditions and passive immunization is therefore inapplicable.

Other acute infective diseases

No reliable means are available of producing active immunity against chicken-pox, rubella, or mumps, and protective experiments with convalescent sera have generally been disappointing. As these diseases are characteristically mild, little advantage can accrue from mitigation of the disease, nor can such an effect be readily demonstrated in individual cases on account of the wide variations encountered in the natural disease.

RECENT ADVANCES IN DIAGNOSIS

Although no entirely new diagnostic method has emerged in recent years, some advance can be recorded in the direction of perfecting the technical details of old methods or in their more precise application. The Widal reaction continues to be the most useful instrument in the diagnosis of the enteric infections; the modification of the test in which Vi antigen is incorporated as well as H and O antigens has served to differentiate between present attack and the immunological response which follows a past stimulus, natural or artificial. Routine cultural examination of blood and faeces in the incubatory period and early stages of the disease is advisable, as evidence of invasion and infectivity may be thereby obtained before clinical manifestations appear.

For diphtheria the recent use of highly selective media and the routine application of animal inoculation tests for virulence have made the diagnosis more precise, but a definite report on a swab is rarely available within 12 to 18 hours. By Mansullo's technique the result may be obtained in 3 hours and by

a further development of the test in 10 minutes. In the former the swab is incubated at 37° C. for 3 hours on tellurite media which growing diphtheria organisms render black from reduction of the tellurite. The rapid test consists in the application of a 2 per cent solution of potassium tellurite to the suspected exudate, which shows black discoloration in 5 to 10 minutes, if diphtheritic, while exudates due to other pathogens remain unaltered. Two recent reports (Tombleson and Campbell; Tomlin) of experience of the latter method in Great Britain have been unfavourable, especially in regard to the large numbers of false positives returned; the conclusion was arrived at that the method was too unreliable to replace the accepted clinical and bacteriological tests of the disease.

The cough-plate has firmly established itself as the most reliable laboratory method in the early diagnosis of whooping-cough. In infants in whom cough may be a trivial feature more success attends the use of the pharyngeal swab upon which organisms are projected from the larynx on introduction of the swab. The search for a reliable test substance to denote immunity to the disease has so far proved fruitless, recent experiments with a specially purified endotoxin (Thompson) suggest that skin sensitivity, which appears about the tenth day of the disease, increases in intensity until the disease reaches its acme, and declines during convalescence, is an allergic phenomenon analogous to the Mantoux reaction for tuberculosis.

RECENT ADVANCES IN TREATMENT

It was inevitable that the new chemical substances, sulphonamide and its derivatives, should be compared in therapeutic efficiency, safety, and ease of administration with established specific remedies, notably immune sera. Later, as the limitations and disadvantages of the new drugs were more clearly ascertained, it was realized that the actions of serum and drug might be complementary, the former supporting and reinforcing the defence mechanism of the body, the latter inhibiting and, under favourable conditions, killing the invading organisms. Even in the treatment of typhoid fever, in which the use of these drugs is theoretically contra-indicated as they may increase the tendency to granulocytopenia characteristic of the disease, the single clear-cut success recorded (Harries *et al.*) was in combination with Felix's V₁ anti-typhoid serum. In certain other diseases, notably in scarlet fever and cerebrospinal fever, the best results have been recorded when serum and sulphanilamide were combined. More recent reports (Bryant and Fairman; Osborn) suggest that even severe meningococcal infections respond promptly to very small doses of M & B 693 alone, orally, or parenterally when oral administration is impracticable because of dysphagia or gastric irritability. In puerperal sepsis and erysipelas serum therapy had been abandoned before specific chemotherapy was introduced, and in these two diseases it so happens that the latter found its earliest and in some respects its most brilliant application. In the treatment of measles and whooping-cough immune sera have little place but sulphanilamide has been found to be effective in reducing the incidence of invasive complications, such as broncho-pneumonia and suppurative otitis media, which are commonly due to haemolytic streptococci and pneumococci, and in improving the prognosis when these complications are established (Thompson and Greenfield). It may well be that events will show that the published results flatter these drugs; apart from the natural tendency to place on record only findings which are regarded as favourable, there has been a general lack of observance of the elementary rules of biological assay in the employment of these drugs in human disease. Moreover, not only in respect of puerperal sepsis for which prontosil was first employed, but also in several other infectious diseases there are grounds for believing that both clinical severity and case-fatality had been showing a distinct and more or

less progressive decline prior to the introduction of these drugs. Caution is therefore still needed before a final verdict is possible.

LINES OF FUTURE DEVELOPMENT

In time it may be found possible to replace crude antigens by purified substances possessing high immunological properties and free from undesirable reactions, which could be combined into a single polyvalent inoculum capable of conferring immunity against all the diseases for which each component is specific; it may be found more practicable to destroy or render innocuous the micro-organisms pathogenic to man, or alternatively to debar them from access to non-immunes; or, as appears to be taking place, although the nature and amount of change are not readily measurable by ordinary clinical and bacteriological methods, improvement in the general standard of nutrition and hygiene of the population may render these procedures unnecessary. The ultimate goal will probably be reached by advancing along all three roads.

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Q FEVER

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DEFINITION

Q fever is an acute febrile disease found chiefly among abattoir workers and farmers in Southern Queensland and due to infection with *Rickettsia burneti*.

AETIOLOGY

The infection known as Q fever first attracted attention because of the occurrence of frequent clinically similar illnesses amongst workers at one of the Brisbane abattoirs. Laboratory investigations were begun in 1935, and since then more than a hundred cases have been observed in Queensland, the majority (70 per cent) in abattoir workers. The susceptibility of the guinea-pig to experimental infection (Derrick, 1937) provided a method of recognizing the disease, and has made possible most of the subsequent investigations. Blood taken from a patient during the febrile period and injected into normal guinea-pigs provokes a characteristic temperature response, and the fever-producing agent can be transmitted indefinitely from animal to animal. A guinea-pig which has once reacted fails to do so after a second inoculation of infective material. Infection can also be produced in mice, and smears from the liver and spleen of infected mice may show large numbers of rickettsiae from which relatively pure suspensions of rickettsiae can be prepared and used as an agglutinating emulsion. By the application of these experimental methods it has been shown that *Rickettsia burneti* is a natural parasite of the bandicoot *Isodon torosus* Ramsay and possibly of other wild rodents or marsupials. This bandicoot is a small ground-living marsupial, very common in many parts of Queensland. Infection is spread from one animal to another by ticks of the species *Haemaphysalis humerosa* Warburton and Nuttall. This tick is found along the Northern and Eastern seaboard of Australia, and, though the bandicoot appears to be its principal host, it has been found on a number of other animals. Experimentally, it will feed on a human subject, and it is possible that most human infections are transferred by tick bite. Very few, however, of the patients remember being bitten by ticks, and this mode of infection could be completely eliminated in the case of some human laboratory infections in Melbourne. In Queensland the great majority of cases have occurred in persons employed at meat works (70 cases) or on dairy farms (22 cases), suggesting that an ectoparasite associated with cattle is the important vector. The crucial epidemiological problem of how most human infections occur therefore still awaits solution.

The rickettsia of Q fever differs from all the other members of the group which cause human disease in failing to induce the appearance of agglutinins against one or other of the *Proteus X* strains. In all other respects it is a typical

rickettsia, not cultivatable apart from living cells, and showing the characteristic delayed growth in tissue culture.

Davis and Cox encountered in Montana an infection of ticks which is due to a rickettsia similar to, or identical with, *R. burneti*, and a probable case of laboratory infection with the Montana strain has been reported (Dyer). This opens up the possibility that Q fever may occur over a much more extensive region than is at present recognized.

MORBID ANATOMY

As the uncomplicated disease is not fatal in human beings, there is not any direct information about the morbid anatomy of the infection. The spleen may occasionally be palpable, and there is often tenderness to deep pressure in this region, suggesting some inflammatory changes there. In the guinea-pig the only constant sign is enlargement of the spleen; occasionally there are small haemorrhages in the caecal wall. Infected mice regularly show enlarged spleens, and the liver is often increased in size and may show macroscopic evidence of damage. Smears from both organs usually show large numbers of rickettsiae. In the spleen the rickettsiae are present in relatively large micro-colonies within cells of the splenic pulp. Sections of the liver show variable degrees of focal necrosis. Rickettsiae are almost exclusively found in the Kupffer cells lining the sinusoids, the parenchymatous cells being free of them. Rhesus monkeys are also susceptible to infection, and show a well marked febrile response, but no pathological studies of this animal have been made. In all three species there are no obvious symptoms apart from fever, and the infections are never fatal.

CLINICAL PICTURE

The length of the incubation period is not known with certainty, but consideration of the history of persons who became ill after ceasing work at a Brisbane abattoir known to be a centre of infection, makes it likely that the incubation period may extend to at least forty-four days. In guinea-pigs the incubation period ranges from one to eighteen days, depending mainly on the size of the dose administered, and it is probable that the incubation period may vary to a similar extent in human beings.

The illness commences acutely, and within a day or two of the first premonitory symptoms the patient is in bed quite ill. The temperature rises rapidly to between 102° and 104° F. and remains high. Some charts show large daily remissions. These are in part due to the use of antipyretic drugs to relieve the headache, but it is doubtful if this explains them all.

With regard to the duration of the fever there are two distinct types. In about 75 per cent of cases the fever lasts from six to ten days, and its termination is fairly rapid. Occasionally, though not as a rule, the termination is rapid enough to be called a crisis. In the minority of cases the duration is longer, and the defervescence gradual. In one case the duration was seventeen days, and in another twenty-four days. In another case the course was extremely prolonged. The fastigium of the fever lasted till the twenty-third day, and the fall thereafter was very gradual. There was still a slight evening rise of temperature in the ninth week.

Occasionally there is a relapse. In a series of twenty cases a relapse occurred in two. It began after one or two days of normal temperature and lasted six or eight days.

The outstanding symptom is headache. Practically all patients have complained of this, and with most of them it has been the chief complaint. They have spoken of it as severe, intense, and raging. It has often been associated with insomnia.

Shivers are commonly present at the onset. Several patients have had definite rigors. Sweating is frequent and due in part, but not entirely, to the drugs used to relieve the headache.

Photophobia is usually present, the patient lying with eyelids half closed to exclude the light.

Only three patients out of sixty have had a definite rash. The absence of a characteristic rash in Q fever is an important point in the differential diagnosis from murine typhus.

A feature of Q fever is the slow rate of the pulse at the beginning of the illness in comparison with the height of the fever. The slow pulse-rate may be of some help in the diagnosis, although other fevers also show it.

There is often tenderness to deep pressure in the region of the spleen, indicating no doubt some inflammation in that organ. Occasionally (two cases out of seventeen) the spleen may be palpable.

Other symptoms which occasionally occur include nausea, vomiting, abdominal distension, cough, and epistaxis. Constipation is the rule. The urine almost always contains a little albumin at the beginning of the fever.

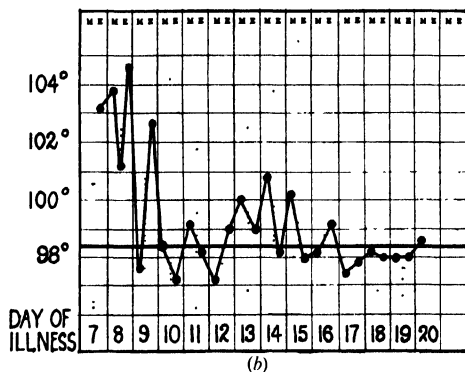
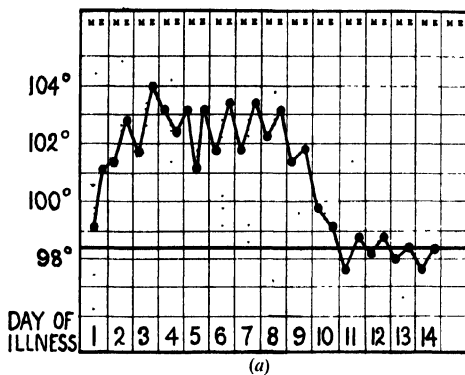


FIG. 3.—Temperature charts. (a) Characteristic course of uncomplicated Q fever; (b) Q fever with a short relapse

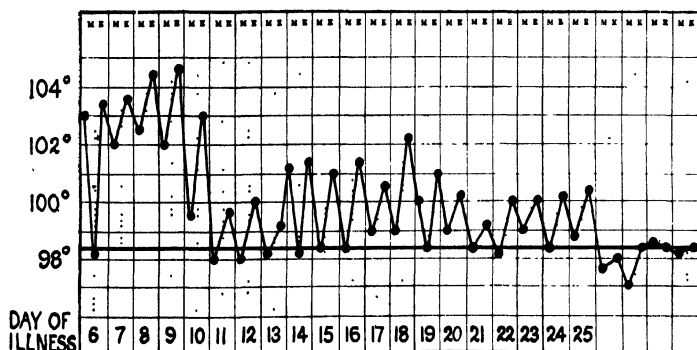


FIG. 4.—Temperature chart in Q fever, showing an unusually prolonged course.

The leucocyte count is at first unaltered. At about the time of defervescence a relative lymphocytosis develops and persists for several weeks.

COURSE AND PROGNOSIS

In young people Q fever usually runs a short course of six to ten days, recovery is prompt, and the patient is often back at work in three to four weeks. In older patients the disease tends to be more severe, and the longer course of illness, ending by gradual lysis, has been more often seen in those over 50. In severer cases and in older patients convalescence is often slow; one man was away from work for five months.

Two patients out of the 105 diagnosed cases died. The first, aged 62, was suffering also from chronic pulmonary tuberculosis. He died on the fifteenth day of illness, apparently from toxæmia. The spleen was considerably enlarged (16 oz.). There was no pneumonia. The second was aged 50. He died on the eleventh day of illness. At the necropsy extensive consolidation was found in the lungs.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Diagnosis can be made with certainty only by laboratory tests, of which three are available.

(1) *Inoculation of guinea-pigs*

Blood or urine from the patient is injected into guinea-pigs. The blood should be taken during the febrile period. The specimen may be citrated to facilitate subsequent injection. If it is allowed to clot, the serum is separated and the clot is ground up for injection. Samples of blood may be sent from a distance as they retain their infectivity quite well for short periods.

If Q fever is the probable clinical diagnosis, and the blood is obtained at the height of the fever, it should be inoculated into two guinea-pigs, one new one and one rendered immune to Q fever by an earlier attack. A characteristic febrile reaction in the new guinea-pig, and none in the immune one, will establish the diagnosis of Q fever.

If the blood to be tested has been inoculated into one guinea-pig only, and it reacts with fever, then its blood or liver is used for the inoculation of a test pair.

The virus may also be present in the urine of human patients, but with urine the results of injection are much less consistent than with blood. It is noteworthy that the successful results with urine are obtained late in the illness or during convalescence. One patient still had the virus in the urine after being afebrile for nineteen days, and actually back at work.

A febrile reaction in an inoculated guinea-pig would not in itself be sufficient to sustain a diagnosis of Q fever. Somewhat similar reactions may be caused by a number of diseases, such as typhus, leptospirosis, and undulant fever. It is essential therefore that the specificity of the reaction should be checked by immunity tests.

(2) *Inoculation of mice*

The inoculation of the patient's blood into mice, and the subsequent finding of rickettsiae in their spleens is a possible method of diagnosis, analogous to the method used for diagnosing psittacosis. This method has only been used on two occasions and is probably less satisfactory for general diagnosis than either guinea-pig inoculation or the agglutination test.

(3) *Agglutination of rickettsial emulsion*

Rickettsial emulsions for agglutination are prepared from the spleens of infected mice at the Walter and Eliza Hall Institute, Melbourne. Such

emulsions are specifically agglutinated by sera from patients from about the tenth day after the onset of illness. The agglutinin titre rises considerably between the tenth and twentieth days, and detectable agglutinins may be present for a year or more after infection. The titre reached varies considerably, but any agglutination at a final serum dilution of 1 : 10 or higher may be taken as specific.

It is unfortunate that none of these tests gives rapid results, and their main value is for retrospective diagnosis or for epidemiological studies.

In South Queensland the principal febrile conditions which need consideration in the differential diagnosis of Q fever are typhoid and paratyphoid fevers, murine typhus, leptospirosis, and influenza. A number of rarer types of fever may also have to be considered, such as psittacosis, dengue fever, undulant fever, and malaria, and it will be necessary to exclude the various forms of fever due to local infections, pneumonia, pyelitis and so on. Clinically, the features of Q fever which may have diagnostic significance are the following: (1) occupation of abattoir or dairy farm worker; (2) an acute onset more rapid than that of enteric fever, but less acute than that of influenza or leptospirosis; (3) the dominant symptom of severe headache; and (4) the characteristic course of six to ten days, and finally the absence of features typical of other infections. There is as a rule no rash, no enlargement of the spleen, no diarrhoea, and no respiratory signs.

In any serious fever the information necessary for bacteriological diagnosis will usually be obtained if blood, taken at the height of fever, is cultured and inoculated into guinea-pigs, and if another specimen is taken about a fortnight after the onset, and the serum tested for agglutinins against the enteric organisms, *Brucella abortus*, *Proteus* λ 19, and λ .K. and Q rickettsial emulsion. The possibility that agglutinins may have persisted since a previous infection unconnected with the present one must of course be kept in mind.

TREATMENT

There is no specific treatment. The fever must run its course. Fluids given freely by mouth are advisable, and frequent sponging when the temperature is high. The mouth requires frequent cleaning. Sedatives are usually required for the headache and insomnia.

Phenazone, soluble barbitone, or a mixture of potassium bromide and chloral hydrate are useful drugs, but the severity of the headache often requires for its relief phenobarbitone or morphine. Sedatives which are also antipyretics (e.g. aspirin, or mixtures of aspirin, phenacetin, and caffeine) are best avoided, since they bring down the temperature with the discomfort of heavy sweating, and, when the effect is over, the temperature rises again, perhaps with a rigor.

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OTORHINOLARYNGOLOGY

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The birth and development of a form of specialism in medicine is generally associated with the invention of some particular instrument or apparatus, usually for diagnosis, but also for treatment. The laryngoscope, the bronchoscope, and the cystoscope are obvious examples. The practice and dexterity required for the successful use of these instruments justify the speciality of which each has been the parent. Other specialities such as dermatology and gynaecology lack this justification, but it is perhaps to be found in the convenience of hospital administration, and they are therefore still practised with success, and no doubt always will be, by general physicians and surgeons as well as by specialists. More recent specialities, such as thoracic surgery and neuro-surgery, justify themselves on the ground that the difficulty of the surgical technique required demands that its practice be concentrated in the hands of a few surgeons who may in that way become masters of a branch of general surgery associated with peculiar and formidable anatomical and physiological conditions.

OTOLOGY

Next to ophthalmology, otology is one of the oldest forms of specialism, and takes its origin from the invention of the aural speculum by von Tröltzsch. Unless the practitioner has acquired by constant practice sufficient skill to make a satisfactory examination of the tympanic membrane, now much facilitated by the invention of the electric auriscope, and of the nasopharynx, he can scarcely begin to arrive at a sound diagnosis except in an occasional case. There is no reason, however, why general surgeons should not do this, and in fact aural surgery owes most of its fundamental advances to the work of general surgeons who have combined aural surgery with general surgery. The names of Ballance in Great Britain and von Bergmann in Germany will always be associated with the major surgery of the ear.

If custom and convenience now restrict the practice of otology almost entirely to specialists, who may justify themselves by a detailed knowledge and long familiarity with the anatomical peculiarities of the temporal bone, it is none the less incumbent upon such specialists to learn and to base their surgical practice upon the general principles of surgery. That this is not always properly understood is shown by the deplorable custom, seen in recent years with increasing frequency, of closing or attempting to close infected bone wounds with insufficient drainage. An unending series of recurrent abscesses and other infective lesions shows that otologists cannot ignore the general principles of surgery with impunity, and that cavities in the temporal bone possess no immunity from the difficulties which the attainment of sound healing of wounds presents in other bones.

The Carrel-Dakin method of treating infected wounds and the application of crude cod-liver oil to sluggish bone wounds are two methods of treatment insufficiently employed in aural surgery.

Specialism associated with a particular organ must by its nature have a

medical as well as a surgical aspect, although in the past the achievements of otology have been mainly surgical.

Otosclerosis

The pathology of otosclerosis, so common in young women and often leading to a high degree of deafness at a comparatively early age, has been studied very thoroughly in sections of the temporal bone, particularly by Albert Gray and also by F. Nager in Zurich and by O. Mayer in Vienna. Although the outstanding feature is ankylosis of the stapes in the oval window, an observation made more than half a century ago, the researches of Gray showed that there are wide-spread changes throughout the temporal bone, and also in the auditory nerve and the external auditory meatus. The whole organ of hearing becomes involved at some period of the disease.

In the early stages of the disease, before the auditory nerve and the cochlea begin to fail, it seems that the deafness and tinnitus are caused by a rise in tension of the perilymph, and it was found many years ago that, if an opening were made into the promontory or into the lateral semicircular canal, the hearing returned in a dramatic fashion. This improvement in hearing only lasts about ten days and when the opening closes the hearing capacity returns to its previous condition. This tantalizing method of restoring the hearing has led to numerous attempts to create a permanent fistula, in the hope of maintaining indefinitely the improvement in hearing. Although many devices, including grafts in various forms, have been tried, the solution of the problem of keeping the osseous fistula patent has until recently proved elusive. Lempert, however, claims that in 22 out of 23 patients upon whom he operated, the fistula remained open and in 19 a great improvement in hearing was obtained and maintained. Patients retaining good bone conduction were selected and the operation was performed by the endaural route, that is, through the external auditory meatus, enlarged by his method. Using strong illumination and high magnification, the fistula is made in the form of a trough and covered with a thin tympano-meatal flap, which by this method of operating can be fashioned so that it is very thin and is nourished by the vessels in the tympanic membrane. As soon as the canal is opened a drop of perilymph escapes and it is essential not to injure the membranous labyrinth. The technique is very delicate and includes removal of the head of the malleus, which is cut with a special guillotine, but as the fistula test remains positive in these patients it appears that Lempert has surmounted the technical difficulty of maintaining the fistula patent by means of this operation, which has the great advantage that it is completed in one stage.

Nevertheless, this operation does not overcome the fundamental morbid process which produces otosclerosis, though it gives promise of being of great value in carefully selected cases.

Alleviation of deafness

For the present the chief of the two great reproaches to otology, the alleviation of chronic deafness, still remains to be removed, and it is necessary to rely upon improvements in aids to hearing (see p. 100).

Intracranial complications of middle-ear disease

The other great reproach, the high mortality associated with the intracranial complications of middle-ear disease, has in recent years been to a certain extent removed in two ways. The outlook in abscess of the brain has been improved by the recognition of two distinct types. The chronic type of brain abscess commonly associated with old suppuration and cholesteatomatous formation in the middle ear is the type which is connected with the diseased area in the temporal bone by a fistula or a stalk and is often encapsuled. A large proportion of such cases can be drained successfully along this track

after exposing the site at which the suppuration has perforated the temporal bone and the dura mater. Acute abscesses, in which the prognosis is not so good, are produced by an encephalitis which has become suppurative. The recognition of an otogenic encephalitis which simulates cerebral abscess both by its general symptoms and by producing localizing signs, has saved many patients from unnecessary cerebral exploration, for such an encephalitis often subsides without passing to the stage of suppuration. If exploration proves necessary on account of abscess formation, the delay, provided it is not too long, is beneficial, for the abscess has time to become localized and to some extent encapsuled. Such abscesses may with advantage be aspirated, or treated with very small drainage tubes at first, the drainage being gradually increased. Otogenic encephalitis may itself be fatal, but operation is of no benefit in such cases.

In the second place the introduction of the sulphonamide group of drugs has produced a great improvement in the prognosis of both meningitis and the intravenous complications of suppuration in the middle ear. Recovery from meningitis is now commonplace and almost to be expected, and many intravenous infections can be arrested almost at their inception, but it is necessary to emphasize the need for appropriate surgical treatment, including elimination of the primary forms of suppuration, lumbar puncture, and exploration of the lateral sinus when required, since no miraculous effect can be expected from these drugs in the presence of pus locked up in bone, or of suppurative thrombophlebitis.

Aural vertigo

Amongst the non-suppurative diseases of the ear, the control of aural vertigo has been especially studied in recent years. For some the elimination of focal sepsis, for others the control of water metabolism, for others the prevention of salt retention, and for yet others a sufficient provision of vitamin C are the factors leading to the successful treatment of Ménière's syndrome. All this indicates that, when the causes of this disabling malady are sufficiently understood, medical treatment may be effective; but in the meantime operations to abolish the vestibular function appear to be the only effective remedy in many cases. This may be accomplished by a direct attack on the labyrinth but, as some 30 per cent of these operations do not give lasting relief, division of the VIIIth cranial nerve has been advocated and practised with great success. In the absence of raised intracranial pressure in the posterior fossa, this operation can now be performed with very slight risk by an operator trained in modern neuro-surgical technique.

Facial palsy

The disfigurement produced by facial palsy is so severe that, apart from the epiphora, the difficulty in mastication and the loss of expression which accompany it, the self-consciousness and mental depression caused may be so profound as to lead to suicide. A study of the best means of relief or cure is therefore worth while on more than purely cosmetic grounds.

Although most cases make a spontaneous recovery, in prolonged compression of the nerve in the aqueduct, or when the nerve is injured during an operation on the temporal bone and the ends are not placed in exact apposition, or if the palsy is caused by permanent damage to the nucleus in the pons, there is no recovery. In the slighter cases of Bell's palsy or in a mild polio-encephalitis affecting the nucleus, or in a recent palsy caused by suppuration in the middle ear subjected to efficient treatment, the paralysis may pass off in a few weeks or even in ten days. In Bell's palsy, which does not so recover and in which the swollen nerve remains compressed in the aqueduct, decompression of the nerve by opening the aqueduct from the lateral semicircular canal to the stylomastoid foramen and slitting the sheath has been recom-

mended. This may be followed by a rapid disappearance of the paralysis, but if the compression has lasted too long the nerve will be found in the canal shrunken and atrophied, and no benefit will follow. When the nerve is injured directly at operation, recovery follows in about four months if the ends are placed in apposition, but otherwise there is no recovery or at the most partial recovery.

For these paralyses lasting more than six months and showing no signs of recovery, union between the peripheral part of the facial nerve and the central part of the spinal accessory or the hypoglossal has been frequently practised. Recovery of power begins to show itself in about four months, provided the case has been suitably selected. Faradic excitability disappears very rapidly, but the muscles must still react to galvanic stimulation and must not have degenerated into fibrous tissue. The hypoglossal gives the best result, and if the descendens hypoglossi is united to the peripheral end of the hypoglossal there is very little atrophy of the corresponding half of the tongue. The spinal accessory should not be used, as weakness and discomfort in the shoulder are produced and there are awkward associated movements between the shoulder and face.

The results of nerve grafting for numerous injuries of the peripheral nerves during the War of 1914–18 proved so disappointing that for some years the method was abandoned as incapable of giving any result of practical value. In facial paralysis, however, it has been proved to be capable of giving a good result. As in union with the hypoglossal or after simple division and regeneration, there is never any recovery of the frontalis muscle and the rest of the face contracts as a whole. The control over the different regions of the face is lost, but the face is symmetrical at rest, the muscles are capable of strong contractions, and the epiphora is relieved.

Relying upon an observation made by Tello in 1911, Ramón y Cajal believed that the empty channels of degenerated grafts are especially rich in neurotropic substances, whereas in a normal nerve grafted directly these substances, though not entirely absent, are liberated very tardily. For this reason Ballance and Duel used grafts of degenerated nerve to repair defects in the facial nerve, believing that the Wallerian degeneration provided tubules down which the nerve fibres would grow readily, and that more rapid regeneration was obtained in this way. It has been shown, however, by Bentley and Hill that the use of degenerated nerve grafts instead of normal nerve grafts has no influence on the rate of recovery nor on the results. Probably the good results obtained by Duel, which were attributed to the use of degenerated grafts, were due to good technique, for Bentley and Hill showed that the more accurate the approximation between the graft and the ends of the nerve the less scar tissue is formed. They also showed that the factors essential to success are first to avoid the formation of scar tissue, which the newly formed nerve fibres will not or cannot cross, and secondly to use a graft of equal calibre to the nerve which is being grafted. They have found that, if these conditions are observed, a graft of even 3 centimetres in length can be used with success.

The operation can therefore be done by dissecting out the middle cutaneous nerve on the front of the thigh and, without allowing it to degenerate, removing a piece longer than is sufficient to provide the required graft. The damaged nerve is then exposed and the ends freshened with a small very sharp knife to remove any neuroma or scar tissue. The exact length between the ends is then measured with a piece of fine catgut and the graft cut so as to fill the space exactly. The ends are placed in exact apposition without any sutures, but the graft is covered with a piece of gold leaf to prevent any disturbance during subsequent dressings.

It is clear that this method should be used whenever it is practicable to do so, but the claim that it should replace altogether other methods cannot be

upheld, because in very extensive bone destruction when the central end of the facial nerve cannot be identified, or when the paralysis is nuclear, this operation cannot be practised, and it is necessary to have recourse to union with the hypoglossal. It would also be impossible to employ a graft if the injury to the nerve lay between the nucleus and the geniculate ganglion, as may happen in the removal of an acoustic neurinoma. Poppen has recently reported seventeen such cases in which a satisfactory result was obtained by uniting the facial either to the hypoglossal or the spinal accessory. It is necessary therefore to be prepared to employ one of several methods, and if the muscles have so degenerated that they no longer react to galvanic stimulation some plastic operation using strips of fascia lata attached to the temporal muscle is required.

RHINOLOGY

The nose has long been regarded as one of the least satisfactory fields of surgical endeavour, for the maintenance of its physiological integrity depends upon the preservation undamaged of its ciliated epithelium. There is now a general agreement that, apart from the treatment of malignant tumours, the surgery of the nose should be as conservative as possible, and more attention is being directed to other lines of treatment. A study of the protein, bacterial, or other forms of sensitization in sufferers from vasomotor rhinitis is more likely to indicate the way to obtain relief from the nasal obstruction, sneezing, and other discomforts than surgical attacks on the mucous membrane, although such operations, often of a drastic character, have often been performed, frequently owing to a confusion or failure to distinguish between vasomotor rhinitis and infection of the accessory sinuses.

Atrophic rhinitis

Turning to the opposite condition of atrophic rhinitis, the aetiology of which has always been somewhat mysterious, surgical treatment has again proved disappointing and the tendency is to treat it upon more physiological lines. The application of glycerin containing 25 per cent of glucose, with the object of promoting the growth of harmless glycophilic bacteria and creating an environment unfavourable to the growth of the *cocco-bacillus* of Perez, has proved clinically to be of great practical value.

The disease has almost disappeared in Great Britain during the last twenty years, though it was formerly quite common and still is so in many other countries. The victims are mostly young women, and it has been observed that the symptoms often undergo great amelioration during pregnancy. It has been suggested in consequence that the atrophic condition of the nose is due to lack of a hormone, which is believed to be either acetylcholine or a closely allied substance, and beneficial results have been claimed from intramuscular injections of gravidan or gravidol prepared from the urine of pregnant women. On the same principle the use of oestrone has also been recommended both locally and by intramuscular injection to remedy this endocrine dysfunction. Oestradiol benzoate and stilboestrol, the synthetic equivalent, are also being used by intramuscular injection, and it is claimed that this form of treatment gives relief also in some cases of vasomotor rhinitis.

PHARYNX AND LARYNX

Malignant disease

In the pharynx and larynx the treatment of malignant disease still offers the most difficult problem, and this problem has become much complicated by the introduction of radiotherapy. These regions have been selected for a concentrated study of radiotherapy because of the accessibility of tumours

in them. Apart from the nasopharynx, however, the results of simple excision or excision by electrosurgery in the pharynx and larynx compare favourably with those in most parts of the body, so that radiotherapy must show an advance on these results if its general adoption is to be justified. The position is different to that, for example, of carcinoma of the oesophagus, in which even the most daring surgical enterprise can accomplish very little. With regard to the pharynx and larynx the introduction of electrosurgery, the improved technique of lateral pharyngotomy, laryngo-fissure and laryngectomy, the recognition of the importance of dental sepsis and of the proper scope of dissections for removal of lymphatic glands, and the perfection of methods of plastic repair have all contributed to produce a respectable percentage of lasting results.

In 153 cases of cancer in the larynx and lower pharynx treated by operation, 63 out of 98 in the group of intrinsic laryngeal cancer and 19 out of 55 in the group of extrinsic or pharyngeal cancer have remained well for more than three years, and this includes 27 in the first group and 7 in the second which have remained well for more than eight years. Such results, however, are not obtained without training and opportunities for clinical experience, so that the cases should be concentrated in the care of a few in the same way that patients treated by radiotherapy must be under specially skilled supervision. Even so, a large number of cases continue to present themselves in an inoperable condition and will probably always do so, in spite of the cry for early diagnosis. Such cases can naturally be submitted to radiotherapy, so that an accurate comparison of results is not possible. Treatment by radiotherapy, however, shows that some of the patients, even apparently favourable subjects, die within the first few weeks of treatment from an acute reaction to radiation, so that this method of treatment carries a certain mortality with it. In other cases the tumour does not react favourably to radiation, so that the condition of the neck and mucous membrane may be aggravated. In a fair percentage of cases, however, the tumour disappears and there is an apparent *restitutio ad integrum* without the mutilation associated with surgical intervention. These encouraging results have led to more and more patients being submitted to radiation, but actually the results are rarely of long duration and very few of the patients survive a period of three years. Thus 29 out of 416 patients treated by radiation survived three years or more, as reported by the Medical Research Council in *Medical Uses of Radium* (1938). There were no survivals of ten years and very few of five years. Rather better results were reported by the Medical Research Council in *Radium Therapy Research* (1938) but these were only of recent date and it still appears that a large percentage of primary good results prove disappointing when the test of a three- or five-year duration of freedom from disease is applied. It seems therefore that in this region there is still good reason to rely on surgery when possible and to persist in efforts to improve its technique.

That this is so receives confirmation from the results obtained by Coutard, who has come to the conclusion that in intrinsic cancers of the larynx composed of differentiated cells attempts to sterilize the tumour are always followed by radionecrosis, which itself is generally fatal, and that therefore the treatment of such tumours should be surgical. On the other hand, cancers composed of undifferentiated cells are best treated by radiation, because these are never operable, on account of their biological characters.

The results of X-ray treatment have varied in different years according to the proportion of cases in which the tumours have been composed of differentiated or undifferentiated cells. The general average of survival for five years in this series has been 39 out of 142 patients, or 27 per cent. He has noticed, however, as has also been observed in surgical clinics, that there is a tendency for a new cancerous manifestation, i.e. a fresh attack of the disease rather than a recurrence, to appear about the sixth year.

At present probably the best way of managing such cases is to perform a biopsy. If the tumour is composed of well differentiated cells with keratinization, it should be excised. If the cells of the tumour are undifferentiated the case may be treated by radiation or, if treated surgically, the operation must be a total laryngectomy.

Bilateral abductor paralysis

An entirely satisfactory method of treatment for bilateral abductor paralysis of the vocal cords has still to be devised. This condition not only results from disease in the central nervous system, but also from certain peripheral lesions which are capable of causing compression of both recurrent laryngeal nerves, and especially in a small but apparently inevitable number of cases from operations for goitre. There is consequently in the last group formation of scar tissue in close relation to the recurrent nerves.

The simplest method of giving relief to the laryngeal obstruction is by tracheotomy, and if the patient wears a valve, which consists of a small shutter hanging in a tube which can be plugged into the orifice of the tracheotomy cannula, expired air is directed through the larynx and a normal or almost normal voice is retained. However, a number of operations have been devised and tried with the object of restoring the air-way and avoiding the need for the tracheotomy tube. Operations for removal of one cord or part of a cord merely lead to the formation of a band of scar tissue which re-establishes the previous stenosis, and, even when such operations have been performed submucously with preservation of the mucous lining of the larynx, the ultimate results have not been satisfactory. It has also been suggested that the larynx might be split in the middle line and the desired result achieved by propping the two halves apart and fixing a piece of bone or cartilage between them so as to separate the cords. This again has not proved successful.

The experimental demonstration in monkeys that it is possible to restore movement in the vocal cord after division of the recurrent laryngeal nerve by uniting its peripheral end to the side or central end of the phrenic gave some hope that this might prove to be a satisfactory method clinically, the phrenic nerve being used because a nervous impulse with a similar respiratory rhythm passes both to the diaphragm and to the vocal cord. In clinical practice, however, this device has proved disappointing, probably owing to the onset of contractures in the intrinsic muscles of the larynx. In two cases out of five in which this operation was done no movement resulted and the patients, both women, were treated by tracheotomy with a valve; in a third case, a man of 50, in whom the cause of the paralysis was unknown, the right vocal cord moved out into the cadaveric position after division of the right recurrent laryngeal with some improvement in the air-way, but unfortunately the patient succumbed six weeks later to a septic lymphangitis of the arm, unconnected with his laryngeal condition, and there was no opportunity to assess the result of the union between the recurrent laryngeal and the phrenic. In the remaining two patients, both of whom were young women, the bilateral paralysis being due to an operation for goitre in one and of unknown cause in the other, sufficient movement was restored to one cord to enable the patients to lead an active life, one of them being able to dance. In neither case, however, was such free movement obtained as was seen in the experimental animals, and on the whole the results have been rather discouraging. In the human subject it is necessary to divide the phrenic and unite the whole nerve to the recurrent laryngeal because, owing to the shape of the neck, an end-to-side union is anatomically impossible, and also because the whole force of the nerve impulse in the phrenic is needed. It is doubtful therefore whether it is worth while to risk the production of paralysis of one half of the diaphragm in order to obtain this rather problematical result, unless it is reasonably certain that contractures have not occurred; but the operation

has the advantage that it can be performed under local anaesthesia without tracheotomy. It is possible that a somewhat similar effect might be obtained by dividing the inferior constrictor muscle and exposing the fossa piriformis from outside. By removing the posterior edge of the thyroid ala the arytenoid cartilage could be exposed and the vocal process drawn outwards so as to rotate the cartilage and abduct the cord. The vocal process could then be fixed in the abducted position by attaching it with a suture of silver wire or silk-worm gut to the thyroid cartilage, without opening the interior of the larynx. This would effect no restoration of movement, but an improved air-way. King has attempted to obtain abduction of the arytenoid cartilage by exposing it in this way and attaching the omohyoid muscle to it. He claims a good result from this operation, as the omohyoid contracts rhythmically with respiration. His patient obtained a good voice and the air-way was improved so much that the tracheotomy tube could be discarded.

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THE OTONEUROLOGICAL DIAGNOSIS OF INTRACRANIAL TUMOURS

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It is usual for patients in whom an intracranial tumour is suspected to be referred for an examination of the ears and, although the assistance in diagnosis so obtained is limited and is in no way comparable to that obtained by examination of the eyes, important information can sometimes be gained. Many have worked at this problem and have studied the effect of tumours upon the connexions between the inner ear and the brain. However, the investigations of Nylén, who has examined a large series of cases from the Clinic of Olvecrona in Stockholm, are so outstanding that the subject is best presented by giving a greatly condensed account taken from his monograph.

OBSERVATIONS BY NYLÉN

The material investigated between 1926 and 1935 consisted of 737 cases of intracranial tumour, verified either at operation or at necropsy and also by pathological examination; but for various reasons certain small groups were omitted or discarded in presenting the results of examination, and the number of cases left for analysis was 673. The number of supra-tentorial tumours was 433 (64.3 per cent) and of sub-tentorial 240 (35.7 per cent). The material has been treated statistically, so as to separate as far as possible the probable from the certain.

Otoscopic examination must be made to exclude suppuration in the middle ear and to ascertain the state of the tympanic membranes; but with the object of determining the occurrence of more pronounced venous stasis upon one side or other, it yields no relevant information. In most cases of cerebral tumour an increase of intracranial pressure is produced. It may be supposed that this compression would produce increase of pressure and signs of stasis in the labyrinths analogous to those commonly seen in the fundus oculi. This question has been hotly discussed; some authors believe that all vestibular and cochlear symptoms in cases of tumour depend upon increased intra-labyrinthine pressure, others that this only occurs when the tumour is in the temporal bone or its immediate neighbourhood, whilst others deny that it occurs at all. It is probable that, if labyrinthine stasis occurs at all, it is of secondary importance and not responsible for the production of nystagmus or other abnormality, nor is it comparable with the phenomena seen in the fundus oculi.

Hearing tests

The usual hearing tests for voice and tuning forks are applied. Examination with the audiometer was made in only a few of Nylén's cases and is not essential.

Tests for equilibrium

In testing for equilibrium, the patients were examined for nystagmus and for ataxy by the usual tests for dysdiadochokinesis and dysmetria, before applying caloric, rotatory, or positional tests which are in themselves disturbing. Great importance is attached to the demonstration of nystagmus in other positions besides the usual ones of sitting, standing, or lying in bed. The patient lies on his back, on the right or left side (the head and body being moved together), and finally the head is moved backward in the lying position. The last is the 'hanging head position', during which the head is also turned to right and left. In special cases a 'position table' to which the patient can be fixed is used; this table can be tilted into any position. If nystagmus is the same in all positions, it is called spontaneous nystagmus, i.e. nystagmus which is not influenced by the position of the head. Positional nystagmus is described as of Type I when nystagmus is reversed in direction in the opposite position of the head. For this the right and left positions, the hanging position, and also standing are used. Positional nystagmus is described as of Type II when the direction of nystagmus does not change in different positions of the head, but certain positions either induce the nystagmus or profoundly influence the intensity of existing nystagmus.

For the caloric test the method of Kobrak was employed, using 10 to 20 c.cm. of water at 27° C. or 47° C. In some cases the patients have also been tested by rotation in an electrically driven rotation chair, but owing to compensation or the counter-balancing of Ruttin rotation examinations give very little help. The induced nystagmus with the head erect may be quite normal, even though the VIIIth nerve is destroyed by a tumour.

The test for optomotor nystagmus was carried out by means of a rotating cylinder covered with black and white stripes.

It will thus be seen that the examination includes some tests which are neurological rather than strictly otological and it is not easy to define a clear dividing line.

Taking the whole clinical material of 673 cases, disorders of equilibrium were found in 561 and disorders of hearing in 314 cases. Nystagmus was observed in 346 cases, of Type I in 98 out of the 346 cases, of Type II in 181 cases, and spontaneous (without positional influence) in 67 cases. Thus in 279 out of 346 cases the nystagmus has been influenced by the position of the head. This positional nystagmus has been analysed as follows:

Nystagmus in lateral position only	-	-	-	45 cases
„ sagittal-lying position only	-	-	-	34 „
„ head-hanging position only	-	-	-	84 „
„ several different positions	-	-	-	116 „

The caloric reaction was abnormal in 276 of 671 cases examined and negative in 78 of these.

Differentiation between supra-tentorial and sub-tentorial tumours

The otoneurological signs and symptoms have been analysed in order to determine whether any difference capable of statistical proof can be found between supra-tentorial and sub-tentorial tumours. In 433 cases of supra-tentorial tumours there were vestibulo-cerebellar symptoms in 324 cases and cochlear symptoms in 204, whilst in 240 cases of sub-tentorial tumour there were vestibulo-cerebellar symptoms in 237 cases and cochlear symptoms in 163. The following tables show the total incidence of nystagmus and the incidence of positional nystagmus:

	TYPE 1	TYPE 2	SPONTANEOUS	TOTAL CASES WITH NYSTAGMUS	TOTAL CASES WITHOUT NYSTAGMUS
Supra-tentorial (433)	11	103	21	135 31.2 %	298 68.8 %
Sub-tentorial (240)	87	78	46	211 87.9 %	29 12.1 %

	ONLY SIDE POSITION	ONLY SAGITTAL POSITION	ONLY HANGING POSITION	SEVERAL DIFFERENT POSITIONS	TOTAL CASES WITH POSITIONAL NYSTAGMUS	TOTAL CASES WITH NYSTAGMUS
Supra-tentorial (433)	6	11	76	21	114	135
Sub-tentorial (240)	39	23	8	95	165	211

In addition the caloric reaction is much more often negative in sub-tentorial cases, whereas in the supra-tentorial it was even hypersensitive in 106 out of 431 cases. Reduced hearing is more frequent in the sub-tentorial group and total deafness is common, whereas there was no case of total deafness in the supra-tentorial group.

Symptoms associated with specific tumours

The incidence of the various signs and symptoms has been further minutely analysed according to their association with the different kinds of tumour in their typical localizations.

Acoustic neuroma

In 95 cases of acoustic neurinoma there was nystagmus in 94 cases, vertigo in 72 cases, and reduced hearing in 86 cases with tinnitus in 55 cases. Vertical nystagmus was common and especially pronounced in 11 patients, 5 of whom died shortly after the operation, as might be expected if the brain-stem were affected. Inversion of the reaction produced by the test for optomotor nystagmus has been said to be a sign of pressure on the brain system. In this series 16 cases showed abnormal optomotor nystagmus, but it did not appear to have an unfavourable prognostic significance. Owing to counter-balancing rotation examination does not give much help, but if the examination is made with the head bent backward 90° there may be found a loss of rotatory nystagmus following rotation. The points in diagnosis may be summarized thus. Otoloscopic appearances are normal. The onset of tinnitus precedes that of reduced hearing and disturbances of equilibrium. There are deafness or greatly reduced hearing, positional nystagmus or spontaneous nystagmus, negative or hypersensitive caloric reaction, loss of rotatory nystagmus with the head bent backwards 90°. These signs are combined with signs of inco-ordination in standing, gait, and the movements of the extremities. Confirmatory signs are found in optic neuritis, changes in the cerebrospinal fluid, and at the internal auditory meatus, the last shown by radiological examination.

Glioma in the pons and medulla oblongata

Otoneurological examination is of limited value in glioma of the pons. As these tumours are inoperable there were only 8 cases in the series, too small a number for statistical treatment. Disturbances of hearing and equilibrium are common but show nothing characteristic in contrast to the typical crossed

paralysis. Nystagmus was observed in every case. It may appear in the horizontal and the rotatory forms, the most frequent combination being horizontal-rotatory, and horizontal-rotatory-vertical. The nystagmus is often positional in type. In one case paralysis of fixation was influenced by the position of the head. The caloric and rotatory reactions do not give definite diagnostic information, but a caloric reaction in which the quick phase is absent and only deviation is produced should arouse a strong suspicion of a pontine lesion. The signs may be of diagnostic value when combined with crossed paralysis, disturbances of sensation, and paralysis of visual fixation.

Glioma in the cerebellum

The classification adopted is as follows: A. medulloblastoma; B. astrocytoma; C. remaining forms (angioblastoma; ependymoma; papilloma).

A. Medulloblastoma.—Nystagmus was demonstrated in 24 out of 27 cases. In 19 out of the 24 there was a vertical component. In 20 cases out of the 27 the caloric and rotatory examinations gave a normal result. According to Cushing and Bailey, vomiting and headache occur early with optic neuritis and cerebellar ataxy, whereas nystagmus is rare. The explanation of this difference in the series examined by Nylén is probably that his patients were examined in many different positions of the head, whereby nystagmus has been discovered in many cases. Positional nystagmus of Type I was found in 17 out of 24 cases. It is often vertical upwards and downwards.

The signs therefore of cerebellar medulloblastoma are normal vestibular reactions after rotation and caloric stimulation; normal hearing in both cases, vertical nystagmus mostly positional in type, in addition to symptoms of incoordination, especially in gait. If, in addition, abnormal posture of the head and optic neuritis are present in a young person, the diagnosis of a tumour in the vermis and in the fourth ventricle is confirmed, and it is probably a medulloblastoma.

B. Astrocytoma.—Auditory symptoms are uncommon whereas giddiness and disorders of equilibrium are common. There were 32 cases in 22 of which nystagmus was observed. Twenty showed positional nystagmus, 10 of Type I and 10 of Type II, and in 2 cases it was spontaneous.

The characteristics are normal caloric and rotatory reactions with normal hearing with positional nystagmus of either Type I or Type II, most frequently in several positions of the head, associated with incoordination in gait and other signs of ataxy occurring in a child or young person. The syndrome closely resembles that of medulloblastoma.

C. The remaining forms of glioma in the cerebellum.—There were 50 cases in this group. Here again disturbances of hearing are rare, whereas vertigo and disturbance of equilibrium are frequent. Nystagmus was found in 39 out of the 50 cases. In 22 out of the 39 the nystagmus was of Type I, in 13 of Type II, and in 4 spontaneous.

In 33 out of the 50 cases the caloric reaction was normal. In the 17 abnormal reactions it was negative in 3 only. In one case ocular deviation appeared after the caloric test.

Out of 13 examined by the rotation test all except one showed normal post-rotatory horizontal nystagmus, but with the head bent backwards 90° only 7 reacted normally.

Although slight differences were found in the results of caloric stimulation and of the hearing tests, these were not frequent enough to be capable of statistical proof, and the general picture is the same as for astrocytoma and for medulloblastoma.

It was hoped that, disregarding pathological differences, an analysis of the incidence of the signs and symptoms on an anatomical basis might serve to distinguish between tumours in the vermis and tumours in the cerebellar hemisphere, but here again the differences in the incidence of the symptoms

corresponding to the various localizations were not capable of statistical proof and were not so great as to be even probable. The most that can be said is that the occurrence of a vertical component in the nystagmus is in favour of a localization in the vermis. Actually the tumour is very rarely situated exclusively in the vermis or exclusively in one hemisphere, but generally affects both and besides penetrates more or less into the fourth ventricle.

Whether the tumours are grouped according to pathological characters or anatomical localization, statistically proved or probable differences in the symptomatology do not exist.

Glioma in the corpora quadrigemina and pineal body

There were 34 cases in this group. Tinnitus was noted in 10 cases and subjective reduction of hearing in 4. Giddiness and disturbances of equilibrium were more frequent. Nystagmus was observed in 15 cases, of Type I in 3 cases, of Type II in 7 cases, and spontaneous in 5. A vertical component was common.

The caloric reaction was normal in 17 cases. In the 17 abnormal cases the reaction was hypersensitive in 12 and in one was negative on both sides.

The rotatory test was applied in only 8 cases with the head erect. Five of these gave a normal reaction. In 7 tested with the head bent backwards 4 gave a normal reaction.

Reduced hearing is not a common symptom of pinealoma but only appears when the patient is in a serious condition, though it may remain normal when the tumour is very extensive. Disturbances of equilibrium and nystagmus which often has a vertical component with a normal or hypersensitive caloric reaction comprise the otological syndrome, which is not in itself sufficient to make the diagnosis but may be confirmatory in association with other signs.

Glioma in the temporal lobe

This group includes glioma multiforme, spongioblastoma, oligodendroglioma, and astrocytoma. There were 70 cases, 37 on the right side and 33 on the left. Tinnitus, reduced hearing, vertigo, and disturbances of equilibrium occurred in about one-third of the cases. Nystagmus was noted in 26 cases. Two had positional nystagmus of Type I, 21 of Type II, and in 3 cases it was spontaneous. In 18 out of the 23 cases of positional nystagmus, it appeared in the hanging position only. In 19 out of the 26 cases of nystagmus, it had a vertical component. The caloric reaction was normal in only 45 out of the 70 cases. In 12 cases examined by rotation with the head erect the reaction was normal in 11, and in one case hypersensitive on both sides.

The optomotor reaction was abnormal in 7 out of 38 cases tested, which is more frequent than in other localizations except that of pinealoma.

In 36 out of 59 cases examined the hearing was normal. Five cases had bass deafness on both sides; 7 had treble deafness, and 6 had combined treble and bass deafness on the sound side, whilst on the side where the tumour lay 8 had treble deafness and 3 had combined treble and bass deafness.

As the auditory centres are situated in the temporal lobes it might be expected that there would be a characteristic otological syndrome of glioma, but none has emerged from the study. However, it appears that a positional nystagmus vertical downwards in the hanging position only combined with caloric hypersensitivity on both sides indicates that the tumour has a supra-tentorial localization. If these signs are combined with ataxy in one arm, there is probably a supra-tentorial tumour on the opposite side.

The auditory symptoms show nothing characteristic, and consequently the diagnosis of glioma in the temporal lobe cannot be made by otological examination only, but it can be of great value in distinguishing between a supra-tentorial and a sub-tentorial localization. As the temporal lobe belongs to the silent regions of the brain, this is of great importance. Besides headache, vomiting, and optic neuritis, there have been observed in these cases

double vision, disorders of speech, epileptic fits, dreamy states, and hallucinations of smell.

Glioma in the frontal lobe

This group includes glioma multiforme, spongioblastoma, and oligodendroglioma. The total number of cases was 70: 33 on the right side, 36 on the left, and one multiple. Two-thirds of the cases were free from subjective otological symptoms, but 15 patients complained of vertigo and 6 had objective disturbances of equilibrium. A few noticed tinnitus and reduction of hearing.

Nystagmus was observed in 28 out of the 70 cases, in 3 of Type I, in 22 of Type II, and in 3 spontaneous. In 17 cases the nystagmus occurred in the hanging position only.

In 43 cases the caloric reaction was normal. In 18 out of 27 cases with abnormal caloric reaction there was hypersensitiveness.

Seven cases tested by rotation with the head erect showed a normal rotatory reaction. Of these 7, 4 were tested with the head bent backwards and all gave normal reactions.

In 60 cases the hearing was tested. It was normal in 44 cases, and there was nothing characteristic in the cases with reduced hearing.

In these cases faulty pointing, both spontaneous and after caloric stimulation, was carefully studied, because much importance has been attached to it by Bárány and by many others. Out of 65 cases tested 17 showed faulty pointing. The author concludes that as yet the value of faulty pointing in the localization of tumours in the frontal lobe cannot be fully estimated, but it is a common sign in tumours of the frontal lobe.

In about 30 per cent of cases of frontal lobe tumour there is vertical nystagmus downwards, in the hanging position only, normal or hypersensitive caloric reaction on both sides, and faulty pointing, especially in the arm contralateral to the tumour. Although oto-neurological investigation cannot be the determining factor in the localization of a tumour in the frontal lobe, it can help to support the diagnosis and particularly indicate a supra-tentorial tumour contralateral to the side upon which symptoms of incoordination are present.

Otoneurological examination in cases of parasagittal meningioma and of tumours of the pituitary gave negative results and therefore have not been included in this survey.

Conclusion

The possibility of making a clear demarcation between tumours above and below the tentorium is the principal achievement resulting from this investigation and should be of great value because the clinical material has been treated statistically, thus eliminating the element of chance in the incidence of certain symptoms.

Disturbances in equilibrium are clearly of greater importance than auditory disturbances, and the sign which has proved to be of chief importance is positional nystagmus. With a tumour in the posterior fossa the nystagmus is nearly always combined (horizontal, rotatory, and vertical) and is easily influenced by the lateral positions or by several positions. In a tumour of the anterior or middle fossa, on the contrary, the nystagmus is most commonly vertical downwards and appears most often in the hanging position only.

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HEARING AIDS

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THE INSTRUMENTS

There are three types of hearing aid now in use, namely:

- (1) Sound collectors and resonators: horns, speaking tubes, and auricles (all non-electrical);
- (2) micro-telephones;
- and (3) valve amplifiers.



FIG. 5 Auricles A pair of these auricles are usually worn. They are here shown over the hair for demonstration, but are usually worn, by women, concealed under the hair

Sound collectors and resonators

Speaking tubes and trumpets, which collect sound and magnify it to some slight extent by resonance, are still useful because of their simplicity. A convenient modification, because it leaves the hands free, is that form known as auricles (see Fig. 5). These are small horns, bent round to fit against the side of the head, with adjustable ear-pieces which go into the external auditory meatus. They are very useful for slightly deaf school children, for women who can hide them under their hair, and for people who, not being very deaf, are by temperament incapable of coping with wires and batteries.

Micro-telephones

Of the two electrical types of instruments the micro-telephone is the older, having been invented by Alexander Graham Bell. It consists essentially of a carbon microphone, a small light ear-piece, a switch, and a pocket dry battery. Some have in addition a variable resistance, and a few have also a simple amplifier. Micro-telephones are sold under many names and vary chiefly in the quality of the carbon microphone, but also in the number and size of these.

The ear-piece may be replaced by a vibrating rectangular plaque, which can be kept in position against the mastoid bone behind the ear by means of a

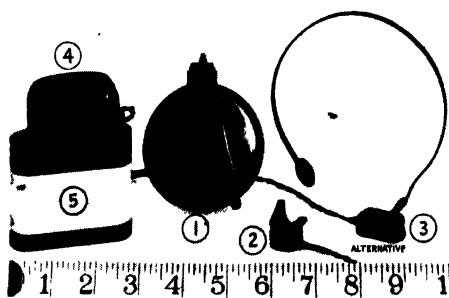


FIG. 6.—Micro-telephone

- | | | |
|--------------|-------------------|---------------|
| | (1) Microphone | (4) Amplifier |
| Alternatives | (2) Ear-piece | (5) Battery |
| | (3) Bone receiver | |

metal head-band (see Fig. 6). These bone conductors may also be fitted to valve amplifiers, but this is less commonly done. The sound amplification of a micro-telephone can be varied slightly by physical changes in the carbon, and by adjustments in the ear-piece, but the changes which are possible are inadequate in extent to match all the different types of defective hearing.

The advantage of the micro-telephone is its portability. Its disadvantages are the noises inherent in the carbon microphone (which are particularly troublesome when the person is moving), the fact that it will not pick up distant sounds, and the expense of the battery upkeep.

Valve amplifiers

The most modern and adjustable type of hearing aid is the valve amplifier (see Fig. 7, *a* and *b*). Since the introduction of midget valves these have become a reasonable equipment for a deaf person to carry and are becoming increasingly so since batteries are becoming smaller and better. Another advance would be made if these were lighter in weight.

These instruments are usually 2- or 3-stage amplifiers, with carbon or piezo-electric ('crystal') microphones, a switch, a volume control, and a small light ear-piece. The details, though ingenious in their attempt to conserve space and minimize weight, have nothing very outstandingly novel from a constructional point of view. Such an instrument can now be obtained measuring approximately 60 cubic inches, and weighing 2 lb. It may be in a single container or in several, so that it can be disposed about the person of a man, if his pockets are of ample size and he is not very particular about changes in his apparent shape. A woman can accommodate it in a handbag.

Some, but not all, instruments have a method of tone control by means of which high, middle, or low tones can be preferentially magnified. Most of these employ devices similar to those used in radio work, but in some cases the adjustment is made by altering the characteristics of the ear-phone. These controls are certainly useful, are sometimes essential, but are often inadequate.

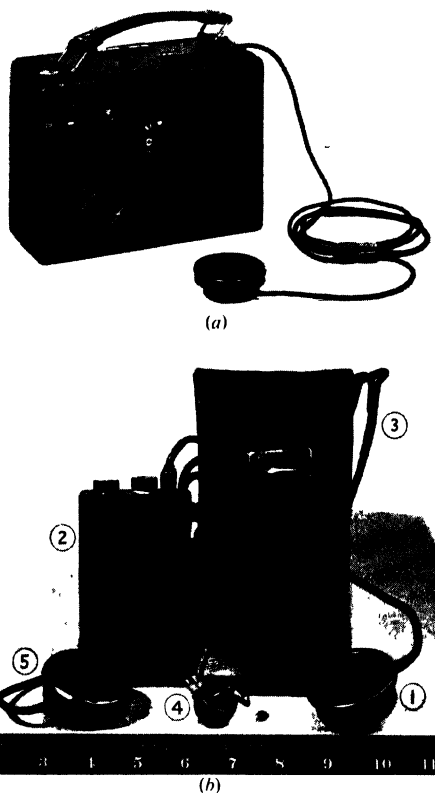


FIG. 7.—(a) Valve amplifier. The piezo-electric microphone is in the same box as the three-stage amplifiers. The head-band which keeps the ear-phone in position has been omitted. (b) Valve amplifier, pocket model.

- | | |
|--------------------------------|------------------------------------|
| (1) Piezo-electric microphone. | (3) Batteries |
| (2) Amplifier and switches | Alter- natives (4) Small ear-piece |
| | (5) Disc ear-piece |

PRESCRIPTION OF HEARING AIDS

It would be convenient if deafness could be divided into classes which corresponded directly with the types of instruments. Unfortunately this cannot be done. For the purpose of fitting aids it is important to consider the physical characteristics of deafness more than its pathology. Different diseases may cause the same effect, as for example, degeneration of the auditory nerve, or the same disease may lead to various results. As an instance, infections starting in the middle ear may cause lesions in both middle and inner ear, and consequently interfere with both the conduction and the perception of sounds. Hence it is always helpful, and sometimes essential, to know the amount of hearing of the deaf person in each part of the auditory scale by air and by bone conduction. This information is easily obtained, given a co-operative patient, a quiet room, and a pure tone audiometer. It must be stressed, however, that the indication of a threshold at a given frequency is not an infallible guide as to the quality of the perception.

Factors influencing types of instrument prescribed

It cannot be said truthfully either that precise prescription of hearing aids is yet possible, or that a universal type of hearing aid is a practical proposition. With regard to a hearing aid, many considerations both human and scientific must be taken into account, apart from the problems caused by those deaf people whose temperament introduces undue complications.

Occupational factors often introduce serious difficulties, as the following examples may illustrate. A domestic servant cannot have any electrical aid always switched on in case the door bell rings. A light-weight jockey cannot carry a valve amplifier in order to hear the starter's instructions. It is difficult to suggest any instrument which is suitable for a fish porter who, when at work, needs to hear instructions as well as to handle heavy wet goods. Moreover, a man who has a moderate degree of deafness due to middle-ear defect, and who wants to hear at lectures, may need the same valve amplifier (about the size of a box camera) as will another man with severe internal ear disease, who can ordinarily hear only a shout in his ear, if the latter is to be able to listen to his neighbour. The same instrument, with its volume decreased, would allow the first man to hear general conversation at a dinner table, but it would not be very convenient in size to be placed on the table or on his knees. Many moderately deaf people, if they can afford it, have two different types of hearing aid, one for close range use, which is more easily worn, and another for functions in large rooms. A clerk who has to answer the telephone often will find a micro-telephone with a bone-conductor ear-piece behind his ear more convenient than one with a disc ear-piece, which must be removed every time before he can use the telephone, even though he may hear a little better with the disc type.

People with middle-ear or conduction deafness can usually hear intelligibly with most types of hearing aid, and whether they prefer auricles, micro-telephones, or valve amplifiers, the last with a carbon or crystal microphone, will depend more on their circumstances and their sensitivity to appearance, adventitious noises, and distorted sounds, than on more scientific factors. The susceptibility of different people varies as much in these as in other things.

Micro-telephones are more suitable for cases of pure middle-ear disease than any other defect, on account of the extent and the nature of the changes in this condition. The effect on the hearing of a patient with middle-ear disease may be that, with a micro-telephone, conversation becomes possible instead of difficult. Some such instruments in which the microphone is rigidly attached to the battery, so that the latter can be used as a handle, are employed profitably by a few people who are far deafer if they place the

microphone within a few inches of the speaker's mouth. This is of practical but limited value, as most people who are as deaf as this have changes in the inner ear. They are much more likely to need magnification of higher pitches than the micro-telephone is capable of providing. Hence they hear distorted speech sounds, so that most severely deaf people trying micro-telephones complain that they 'can hear but cannot understand'.

The art and science of providing the most suitable hearing aid are subtle in the case of people with inner-ear or nerve damage. (It is misleading to call all the cases of defective perception 'nerve deafness'.) It is a matter of knowledge, experience, and trial to determine whether the distortion of sounds of which they complain when using an instrument (and sometimes when not using one) is attributable to an unsuitable hearing aid, or is a necessary consequence of their disorder. Many of these inner-ear cases are high-tone deaf because the base of the cochlea has been affected by disease, or has a deficient blood-supply. Hearing for the middle part of the auditory range (500 to 2,000 cycles per second) may be as defective, or nearly so, as for the high tones, but deafness which is maximal in the 'low' 50 to 200 c.p.s. range is so rare that for practical purposes it can be ignored. It must also be realized that there is a large variety of acoustical conditions covered by the term 'high-tone deaf'.

Few people with inner-ear damage can hear satisfactorily with micro-telephones unless their ability to discriminate distorted speech sounds is unusually good. A valve amplifier in some form is essential both because of the greater power and their greater acoustical adaptability. Its advent has entirely altered the social outlook for such people.

Aids for deaf-mutes

A special note must be added about deaf aids in relation to deaf-mute children. There is a large gap between the degree of deafness at which speech



FIG. 8.—Valve amplifier with multiple ear-phones in use in a school for deaf children. The instrument can be used for magnifying the teacher's voice, or for transmitting broadcast programmes or recorded music. Each child has a volume-control on her desk. Tone-controls are provided, and the box containing these can be seen on the cupboard behind the instrument

will not be heard, and therefore not acquired naturally, and complete deafness. Deaf-mutes are of varying degrees between these limits, few (perhaps 3 per cent) being completely deaf. A pure tone audiometer is of incalculable

value in determining what residues of hearing these children have. It is not usually possible to do more than guess in the case of infants, but a reliable test may be obtained from most children of seven, and from some intelligent children of five and six. Teachers of the deaf have long realized that the slightest trace of residual hearing was of value for the acquisition of speech of natural tone, and have used close individual tuition and speaking tubes, when opportunity occurred. The introduction of valve amplifiers into the class-rooms of the deaf (see Fig. 8) is bringing about a revolution in the education of these children. Experience in this country is still young in this matter. It is certain that a new world is opening to a great many deaf children, although only time will show how far the smaller scraps of hearing will be of real service. For these children it is one thing to hear, and another to appreciate the significance of what they hear, and their speech education is still a slow process requiring skill and patience.

TESTS WITH HEARING AIDS

The medical history and examination, the determination of the auditory threshold for air and bone conduction, and a knowledge of the deaf person's circumstances and requirements, will to an experienced adviser form a valuable guide as to the type of hearing aid which is most likely to suit, and the manner in which its tone should be adjusted for, the patient. Sound-volume control will be regulated by the patient himself, according to the loudness of the speaker's voice, and his distance from the latter.

The final test of the suitability of the instrument will naturally be the practical determination of how much the deaf person can hear with it. Now, this is not so easy to assess as might be supposed, as a deaf person becomes more accustomed to the instrument as time goes on. It is a common clinical experience for a deaf person suffering from severe inner-ear disease, having been given a valve amplifier adjusted to his requirements as well as possible (though usually not according to the scientific ideal), to tell the doctor that he cannot understand a word that is being said. If the instrument is left switched on, and the adviser goes on talking to someone else in the room, the deaf person is often joining in the conversation within ten minutes. This phenomenon has been abused sometimes in commercial circumstances by telling a deaf person that he will hear well with an instrument with which at the moment he hears nothing, in a time too long to be allowed for a home trial period. In most cases the improvement in the mental appreciation of imperfectly heard sounds occurs quickly, and a home trial of a week is in most cases satisfactory; indeed, a trial of some such period should always be recommended. Any scientific test of hearing ability with an instrument in use for the first time must therefore be of a preliminary character, although a better test can be made later with profit. Tests for the hearing of speech for deaf people have been published by D. B. Fry and the writer.

THE PROVISION OF HEARING AIDS

The public still learns, or thinks it learns, about hearing aids mainly from advertisements. Some of these are pure frauds, particularly those concerning invisible instruments without works. The fee asked for home trial is sometimes much more than the value of the apparatus. Even apart from the frauds, most hearing aids are sold more like patent medicines than scientific products. The development of the subject has come from without the medical profession and is sufficiently technical to have been left outside, to the misfortune of the patient. It will never be possible to prevent people who have an incorrigible love of the unorthodox from dealing with quacks of all

descriptions; but an attempt should be made to protect the poor and credulous who believe that anything in print must be true, and also to provide a reliable source of information for the serious inquirer. The position would be simpler if all the instruments for which extravagant claims are made were valueless, but this is not the case. Many of them are quite scientific in principle, and some are good in detail, but most are sold without discrimination. Testing of hearing which is often carried out by the same firms could be carried out by them well and honestly, but it is the exception to find this done.

Up to the present the usual practice of otologists seems to have been to indicate to the patient a reliable maker or agent, and to advise him not to purchase any instrument without an adequate home trial. The National Institute for the Deaf has attempted to deal with this unsatisfactory situation by keeping a list of approved dealers. Subscribers to the list give the following undertakings:

1. That the most suitable aid indicated by the conditions of the client, whether electrical or mechanical, will be recommended, and that, if no aid appears likely to help, the client will be duly informed.

2. That in the event of the purchaser being dissatisfied with the hearing aid supplied and requesting the return of the amount paid, this will be refunded, less a sum of 7·5 per cent of the purchase price for expenses, provided that the instrument or appliance is returned within one week in good order and condition.

3. That no personal interview with a client at his own home will be sought, unless at the request of such client.

In considering applications for admission to their list of firms recommended to the deaf, the Medical Committee of the National Institute for the Deaf take into consideration the nature of the advertising matter issued, and the general methods of business practised in dealing with the deaf, by the firm or dealer making the application. The Institute reserves the right to remove from their list the name of any firm failing to carry out the above conditions, but accepts no responsibility whatever in this matter beyond advising deaf persons as to the firms who have satisfied the Committee in the manner described in the above conditions. They do not give technical advice or any certificates of reliability regarding the instruments.

In my opinion, the above arrangements do not give the patient sufficient help. The National Institute for the Deaf has received numerous letters of inquiry which bear out this point. Some charities, such as the Royal Surgical Aid Society, now insist that, before they give money to help a patient to acquire a hearing aid, they must have a medical certificate which specifies precisely the type and the maker of the instrument recommended. The decision regarding a hearing aid requires a combination of medical science and an appreciation of human requirements and weaknesses which it is extremely difficult to obtain, even in the best commercial atmosphere. Even if the same advice were given by the salesman and the doctor, it would not have the same effect on the patient.

An impartial collection of hearing aids is particularly necessary at the present time, owing to the rapid development of the electrical aids and the increase in the number of hearing-aid makers. Good hearing aids can now be obtained, not only from firms who sell nothing else, but also from larger concerns which make and sell hearing aids as a side-line to their other business. This may have the disadvantage that the sale of the instruments does not have as much personal attention as is given by the smaller hearing-aid firms, but, on the other hand, the overhead expenses of the firm do not all fall on the buyers of the hearing aids. No single maker or agent has at present a range of instruments which, in my opinion, offers the deaf the maximum degree of scientific compensation and social convenience.

Hearing-aid clinics

A hearing-aid clinic provides a solution to this unsatisfactory state of affairs. At centres where these exist, scientific hearing tests can be made, specialized advice can be given, and proper trials can be carried out with the instrument recommended by the doctor in charge. Although it is true that a deaf person can test for himself whether he can hear or not, no deaf person can try all the possible instruments one after the other. He cannot know when a new commercial name covers a new type of instrument or only a new method of adjustment, or whether it is just the same instrument as is sold by another maker. The deaf person can have the benefit of a home trial with the instrument recommended, just as he can with his random choice. He usually sees the doctor in charge of the clinic again at the end of his home-trial period, so that any adjustments, difficulties, or changes can be made.

Hearing-aid clinics are best held at hospitals, so that advice on treatment may be given, and removal of wax or of ear discharge can be easily effected when necessary. Instruments can be obtained much more cheaply through a clinic than elsewhere, as most manufacturers charge the same price to the hospital as they would to an agent. This makes a difference of about 25 per cent in the price, and often amounts to several pounds. Another, and a very great, advantage of the hearing-aid clinic attached to a hospital is that the help and experience of an almoner are usually available. She can obtain for patients financial help from Friendly Societies and Hospital Contributory Schemes, and can interest charitable societies in necessitous cases.

The solution of the problem of the richer deaf patient will probably be the establishment of facilities for paying patients at the hospitals, as is often done for X-ray work. Such a scheme is already in action at one hospital. In a few years' time, perhaps, the instruments will become more standardized, so that a representative collection might be bought by an otologist with a fair degree of certainty that it would not become out of date too soon; this, however, could not be done at present. Many of the active makers are changing their models every six or nine months.

It cannot be too strongly emphasized that patients should be discouraged from going direct to a hearing-aid dealer. However, at least until hearing-aid clinics are more generally distributed throughout the country, it is unlikely that they will altogether be dissuaded from doing so. If they insist on going, they should be advised as follows:

1. To take a friend with them, and listen to a voice they know, as well as to that of the demonstrator.
2. To move about with the instrument on.
3. To switch the battery on (if it is an electrical aid) and to listen when nobody is speaking, both when they are sitting down, and moving.
4. To try more than one make of instrument of the type they favour.
5. To see that the ear-piece fits really comfortably. Ear-pieces can easily be adjusted to individual requirements.
6. To try a large ear-piece as well as a small one.
7. To insist on a home trial, without obligation to purchase.
8. When at home, to listen to general as well as to individual conversation.
9. To see how long the battery (if any) lasts, and to calculate the cost of upkeep.
10. Not to wear a new instrument for too long a period at first. They will probably make their ears tired, and therefore appear to be more deaf.
11. If, after trial of an instrument, they can hear satisfactorily with it and procure one, but subsequently cease to be able to hear with it, or if adventitious noises develop, they should not conclude that they are getting deafer or that the instrument is inefficient. It should be sent to be overhauled. A simple repair or renewal is probably all that is necessary.

The above advice and general information on hearing aids suitable for distribution to deaf patients can be obtained in pamphlet form from the National Institute for the Deaf.

LIP-READING

Any young deaf person should be advised to learn to understand speech by watching the face, irrespective of whether or not an instrumental aid is advocated. It is an invaluable accomplishment for a deaf person, although not included in a strict definition of a 'hearing aid'. Lip-reading is learned more easily when the patient is slightly deaf, and can be used more and more if the deafness increases. Some learn it unconsciously; others find it difficult even after a course of good lessons and much effort. It seems to be an art rather than a science, and self-discipline in order to acquire the habit of watching the speaker's face is an important factor.

There are good facilities available for learning lip-reading. The London County Council organize afternoon and evening classes for deaf adults, as well as schools for deaf children. The National Institute for the Deaf, 105 Gower Street, London, W.C.1, and the National College of Teachers of the Deaf (Secretary, The Mount, Stoke-on-Trent) both keep lists of private teachers of lip-reading with addresses throughout the country.

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PHARMACOLOGICAL ASPECTS OF THE ENDOCRINES

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Since the article on sex hormones appeared in Volume XI of the *Encyclopaedia*, a number of noteworthy developments have occurred.

ANTERIOR LOBE OF THE PITUITARY

At least two new anterior-pituitary hormones, the growth hormone and the lactogenic hormone, have recently been produced commercially, and a certain amount of clinical evidence has been obtained as to their value.

The growth hormone

This, under the name of antuitrin-growth, is available for injection in the form of 10 rat growth units per c.cm. It is a concentrated preparation obtained by a process of extraction from the anterior lobe of the pituitary and is of use in certain cases of dwarfism.

The presence of such a hormone has been shown to exist by the cessation of growth in hypophysectomized animals, and by the fact that injections of anterior-lobe extract will cause growth to start again. Antuitrin-growth is valuable because it does not contain other anterior-lobe hormones, apart from the growth hormone, in amounts sufficient to have any effect.

It is important to recognize that there are various types of dwarfism, and it is not claimed that this preparation is of any value in cases which do not arise from endocrine disturbance, or in endocrine cases which are not caused by anterior-lobe deficiency. It is essential that all cases should be carefully studied in order that the cause may be exactly determined. Family history, and the pre-natal and birth history of the patient must be considered. A full-term infant who is underweight at birth is very often found to be deficient in the anterior-lobe hormones. A thorough investigation must be made of all other possible causes of dwarfism, and a control period during which a suitable diet is administered and careful measurement records kept is advisable before embarking on endocrine treatment.

Biochemical tests to ascertain whether any other organs are failing to function properly should be made, as it is rare to find dysfunction of the pituitary alone, since it is so closely associated with other endocrine organs. In cases of true endocrine dwarfism early diagnosis is of the greatest importance, because a very great proportion of the total growth occurs before the tenth year. Biological experiments have shown that such growth as is induced by the administration of the growth hormone is merely the continuation and acceleration of normal growth.

Antuitrin-growth is standardized in rat growth units, and is administered by subcutaneous injection in doses of from 2 to 5 c.cm., with a total weekly dosage varying from 6 to 10 c.cm. which supplies 60 to 100 rat units per week. Since most cases of deficiency of the pituitary are accompanied by

thyroid deficiency, the simultaneous administration of dried thyroid is advisable, and Schaefer recommends that it should be given, if possible, even when there is no evidence of hypothyroidism. It is important that no endocrine preparation which will hasten sexual maturity should be given in cases of dwarfism, since, after the closing of the epiphyses, the growth hormone ceases to have an effect on stature. The makers of antuitrin-growth give a warning that treatment may have to be continued over months, and even years, in order to have its full effect.

The lactogenic hormone

This hormone, referred to in Vol. IX, p. 614, is now available in a form suitable for clinical use. It is generally agreed that whenever possible infants should be breast fed, and in many cases in which this has seemed to be impossible administration of the lactogenic hormone has sufficiently stimulated the flow of milk.

The fact that milk secretion is dependent on this anterior-lobe hormone has been recognized for some time. The work of Striker and Grueter, in 1928, and of Riddle, Bates, and Dykshorn, in 1932, established the fact that an extract of the anterior lobe would produce milk flow in animals whose pituitary, thyroid, adrenals, and ovaries had been removed. Later, pigeons were employed for standardization, since it was found that the hormone produced proliferation of the crop gland. It is not, however, believed that the lactogenic hormone is the sole factor concerned in the secretion of milk, and the oestrogenic hormones and progesterone are also necessary to build up the mammary tissues and ducts.

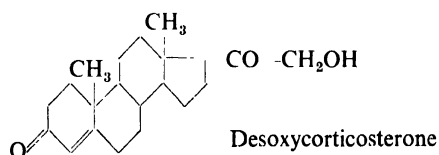
Causes for the failure of lactation may be either physical or psychological. In the normal mother lactation begins when, after the expulsion of the placenta, the high concentration of oestrogenic hormones which inhibit the secretion of the lactogenic hormone falls, and the lactogenic hormone becomes fully active. Lactation is further stimulated by the action of suckling.

It is recommended that the lactogenic-hormone preparation should be given to all primiparae whose milk flow is not adequately established by the sixth or seventh day, and in cases of cessation or diminution of the flow for either physical or psychological reasons.

Physolactin is biologically standardized, and 1 c.cm. contains at least 60 Riddle-Bates units of prolactin. Other active anterior-lobe factors are removed, and it is claimed that the preparation is entirely safe for use in the human subject. For initial stimulation it is administered subcutaneously in doses diminishing from 5 c.cm. to 1 c.cm. over a five-day period, and to stimulate a failing supply it is given for shorter periods.

SUBCUTANEOUS IMPLANTATION OF DESOXYCORTICOSTERONE

This method has already been used clinically for the administration of oestrone, progesterone, and testosterone. Levy Simpson has now reported the successful extension of the method to the treatment of Addison's disease.



He inserted four tablets of desoxycorticosterone acetate, totalling 200 mg., in each of four patients, and found that the effect lasted for about three

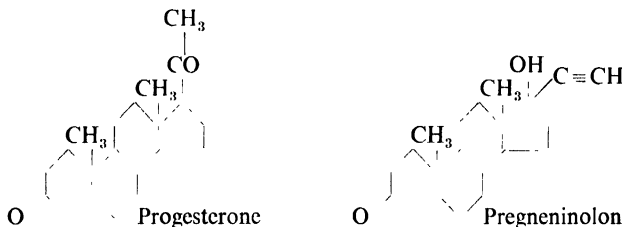
months, as it does in the case of the hormones already mentioned. The advantages of this method are the simplicity of the technique, and the avoidance of the necessity for repeated injections.

Levy Simpson also administered desoxycorticosterone by inunction, and found it to be effective in doses four times greater than those given by injection. The smaller quantities required, however, would seem to render the implantation method preferable, since the substance is very costly.

Dryerre of Edinburgh has described a test which shows the value of the treatment of Addison's disease by desoxycorticosterone; this test is concerned with estimating the urinary sodium elimination. The substance was administered both by injection and by implantation, and it was found that, while injection produced the greater effect, the effect of the implantation of tablets was far more prolonged and was successful in restoring the urinary sodium concentration to normal. The amount implanted was again 200 mg.

ETHINYL TESTOSTERONE, OR PREGNENINOLON

As with the other sex hormones, the clinical use of progesterone has been limited by the fact that it was necessary to administer it by subcutaneous injections. Inhoffen and Hohlweg have succeeded in synthesizing ethinyl testosterone, anhydro-oxyprogesterone, or, as they term it, pregneninolon, and have shown that it has the same biological action as progesterone, to which it is akin in structure.



Although this compound is only about one-third as active as progesterone when injected subcutaneously, it has the great advantage of being many times more active by mouth, and the amount given by injection has only to be doubled to be equally effective orally. Clinical reports on the use of the substance have shown that it will take the place of progesterone in producing menstrual bleeding in amenorrhoea, and that the oral dose must be at least six times the amount of progesterone administered by injection. The chief disadvantage of the substance would seem to be its high cost.

SYNTHETIC OESTROGENS

A considerable number of papers have now appeared on the clinical application of stilboestrol, the synthetic oestrogen described in Vol. XI, p. 94.

All observers are agreed upon the high potency of this material and its power to relieve symptoms of the menopause, and in fact to replace oestrone in every way. There is, however, a very considerable difference of opinion as to the frequency of symptoms of intolerance. At the present time very large quantities of the material have been distributed, and the number of complaints is relatively small. The most pessimistic accounts have come from France, and the publications of Varangot would indicate that, in the dosage employed by him, the symptoms of nausea and vomiting are extremely common. It is possible that at the present time too high a dosage is being

administered, and published results indicate that the menopause can be controlled with a dosage of 0.05 mg. two or three times a day.

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DISEASES OF THE LUNGS AND PLEURAE

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The changes which have taken place in medical methods during the last quarter of a century suggest that the trend of medical progress to-day is towards mechanization, the science of medicine being developed at the expense of the art. This can be exemplified by a study of the methods now in vogue for the examination and treatment of patients suffering from diseases of the lungs and pleurae. It may be profitable, therefore, to pause for a few minutes and take stock of the present position. By looking back we can survey the past and trace the steps by which our knowledge has been acquired. With sufficient insight we can form some opinion as to where we now stand, and with vision we may determine which of the old and new methods are worthy of retention, and in which direction progress is likely to prove most profitable.

THE OLDER METHODS OF DIAGNOSIS

A quarter of a century ago the house-physician, newly appointed to a Chest Hospital, was usually surprised to find that, although he thought himself competent to examine a chest, in actual practice it was most difficult to commit to paper, with diagrammatic representations, the exact signs present in the lungs. It was usually only after about three months of concentrated application that his findings agreed, with a reasonable degree of frequency, with those of the visiting physician. The house-physician soon realized the reason for his early failures.

Clinical examination of the chest is an art, and, in order to acquire this art, an apprenticeship must be served. At the end of his six months' appointment the diligent apprentice had the satisfaction of knowing that he had acquired a special knowledge of a craft which, if duly cultivated, would stand him in good stead for the remainder of his professional career. An appointment as house-physician at a Chest Hospital had thus a very special value which appears to be less evident at the present time, now that less importance is attached to the accurate detection of physical signs. This is largely owing to the routine use of X-ray examinations. Twenty-five years ago radiological methods were not employed in all cases, and the definition of the normal and abnormal shadows seen on the plates was so poor that no great reliance could be placed on their interpretation. Diagnosis was, therefore, mainly dependent upon skill in physical examination and upon judgement in the interpretation of the signs found.

When I was a house-physician at the Brompton Hospital an example which remains indelibly impressed upon my memory occurred in connexion with a patient who had obscure signs at the apex of the right lung. The question arose as to whether he was suffering from a new growth of the lung, and this indeed appeared to be the most likely diagnosis. One of the

Consulting Physicians who possessed in the highest degree the art of physical examination of the chest was called in. He said that he thought the patient was suffering from an apical empyema. On exploring the chest below the right clavicle a loculated apical collection of pus was found and withdrawn. I ventured to ask the physician how he had been able to make this remarkable diagnosis of such a rare condition. His reply was that, according to his experience, in an apical pulmonary tumour the dullness usually extended slightly across the mid line, and that this was not so with an apical empyema.

THE NEWER METHODS OF DIAGNOSIS

Radiography of the chest

Enormous improvements have been made in chest radiography during the past ten years, as can be readily appreciated by comparing a present-day film with one of the older ones. The radiographic details are now sharply defined, good oblique and lateral views can be obtained, and adequate screen examinations made. Further aids to diagnosis have been introduced in the form of tomography, kymography, bronchography, bronchoscopy, the establishment of a diagnostic artificial pneumothorax, thoracoscopy, and thoracotomy. By these means important advances have been made in the early diagnosis of bronchial carcinoma, and the simple adenoma of the bronchus can be differentiated at an early stage from the carcinoma, both of which may give rise to recurrent haemoptysis with collapse of a portion of the lung. These methods have also proved of value in eliciting the presence of a dry bronchiectasis as a cause of pulmonary haemorrhage. The tomogram is helpful in determining the presence and extent of pulmonary cavities or of obstructed bronchi, and the kymogram in differentiating a mediastinal neoplasm from an aneurysm, both of which may give rise to pulsating shadows as seen on screening.

The biochemical methods, recently introduced for determining vitamin C deficiency, are of value in deciding the nature of haemoptysis in certain obscure cases. No useful purpose would be served by detailing here the present possibilities of these newer methods of diagnosis; the general principle suffices that by their help undoubted and valuable advances have been made with surprising rapidity.

The prominence and predominance of the special methods for the examination of the chest have led to the attitude, which is sometimes expressed, that a careful physical examination is a waste of time. It is certainly a waste of time if the examiner has not gone through the mill, and, by laboriously and patiently serving his apprenticeship, acquired the art; but, if he has developed this art and combines it with the newer methods of examination, his opinion will be of far greater value than that of the partially trained physician who trusts to extraneous aids to diagnosis alone. It is astonishing how often physical signs which can readily be detected are overlooked or, if noted, their significance ignored. Examples are afforded by such signs as weak air-entry into a portion of a lung, or by haemoptysis. Weakened air-entry into a portion of the lung may be the first sign of a bronchial carcinoma, and how often is valuable time lost before the diagnosis of pulmonary tuberculosis is made, because the patient who has had a haemoptysis is told that the bleeding has come from a vein at the back of the throat. The best results will undoubtedly be obtained in the future by the chest physician who has been carefully trained in the eliciting of physical signs, who also screens the patient himself, and who finally compares the radiological findings with the results of his previous examinations.

A combination of the older with the newer methods of investigation has led to the recognition of the cause and nature of various illnesses. Thus, in

some cases, unexplained febrile illnesses have been shown to be due to the accumulation of secretion, infected with streptococci, in a localized portion of the bronchial tree, and appropriate treatment has led to a restitution of health. Multiple small shadows in the lung fields, appearing radiologically to be due to miliary tuberculosis, have been demonstrated as visceral lesions of Boeck's sarcoids, as the result of microscopical examination of an enlarged gland or of a cutaneous nodule. Radiological examination of the lungs in children suffering from a persistent cough with slight fever and little constitutional disturbance has revealed in some cases a shadow which may be due to a simple inflammatory lesion—pneumonitis—or to partial obstruction of bronchi with secretion, and which disappears in a short time as the patient is restored to health. Numerous examples of this nature could be quoted illustrating how a careful combination of the older and newer methods of investigation has increased our knowledge of diseases of the lungs and pleurae and enabled us to diagnose them with a greater degree of accuracy.

THE NEWER AND OLDER METHODS OF TREATMENT

Pulmonary tuberculosis

The principles of treatment of pulmonary tuberculosis have passed through a cycle of phases, beginning with rest of varying degrees, and now again returning to rest in as complete a form as possible. In the interval, importance has been attached to climatic treatment, to articles of food such as grapes, whey, or koumiss: we have seen the rise and fall of tuberculin therapy and the use of such substances as sodium morrhuate, calcium or gold salts, none of which has produced dramatic results.

Graduated exercise was in favour at one time, the exercise being increased with the idea of producing a degree of auto-inoculation with tuberculin derived from tubercle bacilli in the lungs, while the disease was still smouldering. To-day it is generally considered unwise to exercise the patient while activity persists. Prime importance is once more attributed to rest as the most important therapeutic agent, the affected lung or lungs being rested as well as the patient.

The greatest advance in the treatment of pulmonary tuberculosis is that which has enabled the basic treatment of rest to be applied locally and more effectively. This implies the use of artificial pneumothorax, by means of which in favourable cases the movements of the affected lung or lungs can be controlled as desired. Surgical procedures for collapsing the lung are sometimes applied when, owing to adhesions, the lung cannot be collapsed by an artificial pneumothorax, but the collapse obtained is not so complete as that produced by a successful pneumothorax.

There is no doubt that to-day the most potent curative agent in pulmonary tuberculosis is rest, both local and general, for prolonged periods of months or years. If all sufferers from pulmonary tuberculosis, and their doctors, would realize that no short cut to cure has yet been discovered, and that the most successful treatment is the least dramatic, the ultimate results would be far better. 'Rest and be saved' is the motto which should be hung on the wall in front of each tuberculous patient's bed. Our future hopes must lie, either in the discovery of a substance which will kill the tubercle bacilli in the body without damaging the patient, or in an agent which will initiate or accelerate the natural processes of healing by fibrosis and calcification.

Bronchiectasis

Turning now to a consideration of the treatment of bronchiectasis we find that the establishment of more accurate methods of diagnosis has resulted in more successful forms of treatment. Thus the use of lipiodol or other

similar radio-opaque substances in defining the localization and extent of bronchiectasis has placed postural drainage on a sounder basis. Knowledge of the exact position of the bronchi affected has enabled correctly angulated postural drainage to be instituted. By the use of a simple wooden frame the patient can become accustomed to lie in the best position for bronchial drainage for many hours during the day, and even to sleep in this position. By these means many brilliant results have been obtained, and, whereas in the early years of this century the fate of the sufferer from bronchiectasis was usually a slow but steady deterioration, to-day we see many patients losing their toxicity *pari passu* with their sputum, and regaining their lost weight with their lost health, until once more they are enabled to enjoy life and work. We may hope that in the future bronchiectasis will become a rarity owing to the adoption of measures which will prevent the incidence of pulmonary fibrosis or collapse, both of which processes could with due precautions such as early diagnosis and adequate treatment be rendered harmless in so many instances.

Sulphonamide drugs

The introduction of the sulphonamide group of drugs for the treatment of pneumococcal and streptococcal pulmonary affections opens a new vista in the possibilities of chemotherapy in such inflammatory diseases. We are now working in an age of chemical and biochemical discoveries which point to future advances in these directions as the probable cure for bacterial and protozoal infections. Just as the bacterial discoveries have enabled us to trace the cause of so many pulmonary diseases, so it seems that in the biochemical laboratories will their remedies be discovered.

Pulmonary carcinoma

Pulmonary carcinoma is still a baffling problem—neither its cause nor its cure has yet been revealed. Thus the use of deep X-rays and of radium has proved so disappointing that no physician can be blamed for not recommending them to the sufferer from bronchial carcinoma. Further research may enable the active rays to be efficiently concentrated on the deep-seated lesions in the chest, with results as good as those obtained with more accessible tumours. Medical art and science have no reason to be ashamed of the progress made during the last quarter of a century, and there is every hope that steady perseverance and research will during the coming years solve many of the problems which now appear so baffling and disheartening.

MENTAL DISEASES

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Recent work has been concerned mainly with the investigation of methods of treatment and their results. The recently introduced types of 'shock therapy' by insulin and cardiazol have been the main topics. Their introduction, however, has stimulated thought and investigation into the pathology of psychotic conditions along biochemical lines, and the attempt at the assessment of the clinical results of shock therapy has drawn attention once more to the difficulties in differential diagnosis, and especially to the lamentable lack of statistically reliable studies of the outcome of psychoses treated in the traditional ways.

MORBID ANATOMY

Theoretical considerations as well as biochemical investigations and a study of the histological changes found after death occurring in the insulin and cardiazol methods of treatment suggest that biochemical factors, and especially those connected with the oxygenation of the nerve-cell, may be important. For example, a study of the biochemical changes induced by pentamethylene-tetrazol (cardiazol or metrazol) shows that, in addition to a fall in blood-sugar after the injection with a subsequent rise above normal for a time, the oxygen consumption rises as much as 40 per cent for several hours after the convulsion. Experiments in rats with the same substance showed a contraction of the blood vessels at the time of the convulsion, with swelling of the brain, presumably accompanied by anoxaemia of the cellular elements (Reid, Steinberg, Liebert, and Finkelman).

Continued treatment with cardiazol (over 20 fits) has been known to be followed by considerable glial proliferation. Similarly, after death from insulin a proliferation of the fibrous glia, chiefly in the white matter, has been found. Typical ischaemic necrosis was only slight (Mackeith and Meyer). In another case of death following insulin there was vacuolar degeneration of the ganglion cell nuclei, especially in the hippocampus and medulla (Kobler). The histological evidence is therefore in favour of an anoxic rather than an ischaemic process as the *modus operandi* of insulin on the brain, and biochemical evidence is thought to point in the same direction.

Anoxia, however, does not seem of itself to be the effective agent. Thus anoxias produced by breathing an atmosphere of nitrogen produced no clinical benefit in four schizophrenics observed by Russell Frazer.

SHOCK TREATMENT

Schizophrenia

On the whole the results claimed appear to show that shock therapy, especially by means of insulin, considerably increases the proportion of schizophrenic patients who are able to make a return to ordinary life. ('Return to ordinary life' includes the cases of both complete remission and 'social'

remissions, i.e. with some symptoms still present but capable of work and of living in ordinary society.) But not all reports are unanimous in this respect, and the question has been raised whether either method acts otherwise than by accelerating recovery in those who would have recovered in any event. There is no question that both these methods, and especially insulin, produce profound changes in the individual patient at the time. These phenomena are of the very greatest interest and theoretical importance, but an attempt at a statistical evaluation is hindered by the comparative absence of reliable statistics of large numbers of cases, one, two, three, and more years after the onset of the actual symptoms.

The largest series of results studied comes from the U.S.A. where J. R. Ross and B. Malzberg gave a '*Review of the Results of the Pharmacological Shock (insulin) Therapy and the Metrazol Convulsive Therapy in New York State*' (unpublished). They report on 1,757 cases treated with insulin and class 11.1 per cent as recovered at the termination of the treatment and 26.5 per cent as much improved. The figures are in general agreement with previous series totalling 1,399 cases, so that the total reported is over 3,000. The duration of the cases from onset varied to as many as 15 years or more. The maximal recovery rate was 26.1 among those with a duration of less than a month. The recovery rate fell to 2.1 per cent among those with a duration of 11 to 14 years. The recovery rate declined as the age at the beginning of treatment decreased.

Allowance must also be made for the fact that a number of the treatments were probably incomplete by present standards. There is a tendency to emphasize the necessity for a complete course of insulin and for not being optimistically deterred by great early improvement from pursuing the course further.

The figures show a shift from one group to another when the cases are followed up. Thus of 139 cases described as recovered at the termination of the treatment, only 73 were so described at the time of the follow up. In other words relapse occurred in 50 per cent of cases classified as recovered at the time of termination: but a number of those described as improved made a complete recovery without further treatment.

A certain amount of confusion is introduced into the discussion by the varying terminology regarding ultimate results, e.g. whether many of the 'much improved' group could be regarded as 'social recoveries'; but even allowing for this difficulty, comparison with results of follow-up studies of cases not treated by shock therapy fails to bring out any very pronounced difference in favour of insulin. As regards cardiazol, Ross and Malzberg's figures show virtually no improvement at all over ordinary traditional results, the complete recovery rates being 4 per cent and 3.5 per cent respectively. Malamud and Render have followed up 177 cases diagnosed as schizophrenia after 5 years and found that 14 per cent showed a complete remission (this figure should be compared with the 11.1 per cent from Ross and Malzberg's series) and 8 per cent showed a social remission. Cheyney and Drewry, following up 2 to 12 years later 500 patients admitted within 6 months of the appearance of symptoms, found that 47 per cent were living outside institutions and that 26 per cent showed either complete recovery or much improvement.

Swiss workers have supported Sakel's claim to a recovery rate for insulin therapy in cases treated within the first six months of between 70 and 80 per cent. But it is difficult to know how to assess this figure when it is remarked that cases classified as 'manic depressive' amount to only 1.5 per cent of admissions to Burgholzli asylum in Zurich, whereas they constitute nearly 15 per cent of admissions to American and British mental hospitals. This may help, as well as differences in technique, to explain the discrepancy between these figures and the 26.1 of Ross and Malzberg.

That great and interesting changes are produced in the course of the individual case is undeniable; that the duration of many cases is shortened is also undeniable; but an appreciation of the real therapeutic value must wait. At least it can be said that some cases otherwise apparently hopeless are made well or nearly well and have remained so up to date. Moreover some very chronic cases are improved or even restored to social life. Meanwhile the results are sufficiently suggestive to make it a duty to advise that one of these methods be tried in the first six months of any schizophrenic illness.

Other psychoses

One of the surprises of these new methods is their apparent efficacy—possibly their greater efficacy—in psychoses with very different characteristics from those in which their usefulness was first claimed. In fact, at present it appears as if the greatest measure of success with cardiazol is obtained with psychoses other than schizophrenia. Manic excitement, for example, has been treated with cardiazol and the excitement has been interrupted; but it has a considerable (some think inevitable) tendency to recur when the treatment is discontinued. It is, however, in depressions that the results with cardiazol are, at least in individual cases (for no large series appears as yet to have been treated) most striking. The field of depression is very wide, and whether it will ultimately prove that those in which constitutional factors clearly preponderate over psychological or incidentally physical ones are the most responsive, remains to be seen. It is in the involutional group, commonly called involutional melancholia, that the best results have been claimed: for example Bennett claims that all of a series of 8 cases of involutional melancholia tended to recover after a few injections of cardiazol. The experience of others bears out this claim in some cases at least. Cooke has recorded success in a few cases of simple retarded depression, of 'chronic hysterical emotional states' and (personal communication) of a paranoid hallucinatory confused state. It may be said at this stage that in any case of depressive psychosis in which the illness has lasted an unusually long time, say three years or more, treatment by a short series of cardiazol convulsions is worth trying.

Insulin has also been tried in conditions other than schizophrenia, perhaps oftener than has been reported. The impression obtained from a visit to the Clinic in Vienna, where the treatment originated, was that treatment began so soon after admission that many cases of mental excitement must have been treated before the diagnosis could have been clear. Apart from its accidental use in excitements that a longer view might have shown to be manic rather than a schizophrenic, its deliberate use in depressive states, especially at the involutional period, has had some success. Insulin shock has also been used in obsessional psychoneurotic states with, it is claimed, success in some instances.

Complications of treatment

To the complications which may be produced by cardiazol must be added an effect on memory—not only an amnesia for events near the time of the convulsion but a more lasting impairment of a minor but nevertheless demonstrable kind. Of 16 cases treated with convulsants, a test confirmed the impression of organic intellectual impairment in 8 of the patients, though 2 of these did not complain of any disability. It is commented that, although the implications of this work are rather grave, it is doubtful whether they out-balance the value of the treatment in a selected case. The risk of memory impairment suggests, however, that convulsants should not be employed, except as an extreme measure, in patients whose livelihood depends on their memory and purely intellectual capabilities (Tooth and Blackburn). This work has yet to be confirmed.

Protracted shock

It had been observed that some cases were accidentally benefited by protracted shock (i.e. persistence of coma in spite of feeding with sugar, and in the presence of a hyperglycaemia). Kraulis decided to apply this to very chronic cases. Protracted shock enables patients to remain in coma for twelve hours instead of one to one and a half hours as in the original method. In order to reduce the danger (Kraulis had two deaths from unintentionally prolonged comas while treating early schizophrenics by Sakel's original method), at the third hypoglycaemic hour, just at the beginning of the coma, small doses (5 grams) of sugar are given by nasal tube. Such small doses have only a slight effect on the depth of coma but hinder the occurrence of lasting damage to the brain. Protracted shock means that the patient remains in coma for twelve hours. Shorter shocks have proved therapeutically of little value in such chronic cases. Of 32 cases which were treated by protracted shock, 10 were of under three years and 22 of over three years' duration. Of the first 10 all gave good remissions, of which 8 were complete. The duration of treatment was on the average half that of cases treated by the usual method. Since Kraulis became aware of the danger of treatment by protracted shock he does not now treat recent cases by this method. Of the 22 old cases, 5 recovered completely and are at work, 6 were discharged improved, and 11 remained unchanged. The number of recoveries is not large, but the otherwise completely unfavourable prognosis made it, in Kraulis's opinion, seem justifiable to continue this method.

OTHER METHODS

Periodic catatonia

Gjessing has shown that in the small group of cases of periodic catatonia (only 3 per cent of all schizophrenics, according to Kraepelin) the phase of stupor or the phase of excitement sets in at either the maximum or the minimum level of nitrogen storage is being reached, and that this relation is very regular. Treatment by emptying the nitrogen store by giving large doses of thyroxine (as much as 44 mg. in 8 days) succeeds in levelling out the condition so that the phases of excitement and stupor are avoided. The nitrogen store is kept low by continuing with dried thyroid.

TREATMENT OF ACUTE MANIC EXCITEMENT

It has recently been claimed that in many cases of acute delirious mania the important factor in producing the acute and dangerous stages are the accompanying dehydration and hypochlorhaemia. It is claimed that the administration of common salt, either by mouth or in uncooperative patients by subcutaneous injection of saline, greatly diminishes the death-rate (Larson).

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NERVOUS DISEASES

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Neurology continues to be one of the most active departments of medicine, and, although in the last year or two there has been no epoch-marking discovery, nevertheless progress has been made at many points. It is satisfactory that some of the most important advances have been in the realm of therapeutics. The introduction of M & B 693 has entirely changed the treatment and outlook in cases of meningococcal and pneumococcal meningitis; sodium diphenylhydantoin has brought an advance in the treatment of the more severe cases of epilepsy and, abroad, nicotinic acid promises to abolish the scourge of pellagra. In the following pages no attempt has been made to give a systematic review of progress in all sections of the neurological field: the aim has been rather to notice such work as affects the present position of neurological theory or practice, or which seems to indicate lines of future development.

ANATOMY

On the pure anatomy of the brain there has been no work of great importance as affecting medical practice in the period under review.

The blood supply of the spinal cord has been investigated by Bolton. This subject, though of great importance clinically, has been to a great extent neglected since the researches of Adankiewicz (1881) and Kadzi (1889). Bolton, using modern injection methods, has confirmed their main descriptions and made new discoveries. The anterior spinal artery, formed ordinarily by the junction of branches given off by the two vertebral arteries in their intradural portions, is reinforced by lateral branches derived from the intra-vertebral portions of the vertebral arteries. The blood supply thus obtained reaches only as far as the 1st or 2nd thoracic segment, and at this level there is an important lateral tributary from the corresponding intercostal artery. Below that level the supply comes from a varying number of vessels arising from the intercostal and lumbar arteries, but is dominated by the contribution from one relatively large vessel situated usually at the level of the 8th or 9th thoracic segment. The anterior spinal artery becomes very small just above the point where a large lateral vessel joins it, and much wider below, thus facilitating a downward flow of blood. The posterior spinal arteries are formed above by branches from the vertebral arteries or from the posterior inferior cerebellar arteries and the flow of blood in them is downward only as far as the lower cervical segments. Below that level the flow of blood is upwards and is derived from the terminal lateral branches of the anterior spinal artery and reinforced by vessels from the intercostal arteries. Within the cord the region of supply of the posterior spinal arteries is limited to the posterior halves of the posterior columns and posterior horns, the anterior spinal artery supplying the rest of the cord, both grey and white matter. The bearing of these observations on certain findings in pressure lesions of the cord is discussed in Bolton's paper.

PHYSIOLOGY

The more academic physiology has been concerned chiefly with the continued study of the cerebral cortex and its relation with underlying structures and the exploration of the vegetative nervous system.

The cerebral cortex and basal ganglia

In connexion with the cerebral cortex Adrian, making use of a process of facilitation, has obtained discharges from the cells of the motor cortex of a frequency hitherto unsuspected—namely, at the rate of several hundreds per second. Dusser de Barenne and McCulloch in a series of brilliant experiments have illustrated the functional interrelations of the motor cortex, the nucleus caudatus, and the optic thalamus. Working with macaque monkeys they began by recording the changes of potential in various parts of the cortex after local strychninization, i.e. the application of strychnine solution to a few square millimetres. In one series of experiments they found that strychninization of an area which they call 4 S, immediately anterior to the precentral gyrus (area 4 of Brodman), suppressed the normal discharge from area 4 recorded in the electro-cortico-gram (ECG). This suppression was not mediated by any direct connexion because it was not prevented by an incision between 4 S and 4. It was, however, prevented by the undercutting of the area 4 S, which indicated that the suppression involved connexions to some sub-cortical structure. In subsequent experiments this structure was identified as the caudate nucleus, and evidence was obtained that the caudate nucleus exercised some controlling influence over the activity of area 4 (the precentral area). It appeared, however, that this control was not exerted directly but through the medium of the thalamus. It was concluded that the striatum, more particularly the caudate nucleus, does not function independently of the cerebral cortex but, on the contrary (i) specific areas of the sensori-motor cortex directly influence, excite, or activate, the caudate nucleus, and (ii) the activity of the caudate nucleus influences or 'brakes' (albeit indirectly via the thalamus) the activity of other specific areas of the sensori-motor cortex. Closely related to this work of Dusser de Barenne and McCulloch are the findings of Mettler, Ades, Lipman, and Culler of whose experiments, however, only a brief preliminary report is available. These authors claim to have obtained from stimulation of the corpus striatum an inhibitory effect on movements initiated by stimulation of the motor cortex.

In another series of experiments involving local strychninization of the sensory cortex Dusser de Barenne and McCulloch obtained evidence of the existence of cortico-thalamic fibres. By taking records of potential changes in the thalamus (electro-thalamo-gram) it was found that a portion of the thalamus which was in functional connexion with a particular part of the body was 'fired' by the local strychninization of that subdivision of the sensory cortex which subserves sensation of the same part of the body.

The vegetative nervous system

In the realm of the vegetative nervous system, many experimenters have been occupied with the observation of reflex effects, and in Great Britain a number of studies on this subject have been published from Carmichael's laboratory. It is evident that, in general, reflexes involving the autonomic system are mediated by the spinal cord. The question whether there are reflexes in the sympathetic chain and ganglia is still answered essentially in the negative. Bolton, Williams, and Carmichael reported two human cases of spinal cord lesions in which the sympathetic ganglia and also the posterior root ganglia were intact. None of their observations on the lower extremities indicated reflex vasomotor responses mediated through the sympathetic chain ganglia. Marquis and Williams, working in the same department, on the vasomotor

responses to painful stimuli in subjects with lesions in different parts of the sensory conducting systems, concluded that in man the ascending pathway for the reflex vasomotor response to somatic stimulation was the spino-thalamic tract and that the vasomotor reflex arc was complete in the brain-stem below the level of 'the sensory thalamus'.

Various workers have studied the reflex effects on the vasomotor apparatus of afferent impulses from the respiratory tract. Bolton, Carmichael, and Stürup showed that when deep breathing occurs in man there is a vaso-constriction in the fingers; they attributed this to afferent impulses passing along the intercostal nerves. The roles of the receptors in the carotid sinus and carotid body in vasomotor regulation and in the control of respiration have given rise to numerous papers.

McSwiney and his co-workers have studied the ascending pathways traversed by impulses from visceral (and somatic) afferent nerves which produce pupillary dilatation. The central pathways for both appeared to be identical and were found in the lateral columns of the spinal cord. Afferent impulses in the vagi and splanchnic nerves were traced from the stomach and duodenum, while from the jejunum and ileum they were mainly in the splanchnics.

Transmission of nerve impulses

The problem of the mode of transmission of impulses along nerves and over synapses and neuro-muscular junctions is still unsettled. Most workers have accepted the evidence in favour of chemical transmission. Fulton has expressed the intermediate view that acetylcholine is a by-product of nerve metabolism and that its presence affects the resting threshold of neurones, while the work of Lorente de Nó on oculo-motor motor neurones narrows the time limit of synaptic delay to such a degree (0.5 to 0.9 m. sec.) as to make it extremely doubtful whether a chemical transmitter could be removed with sufficient rapidity, and so indirectly supports the view that transmission is actually effected by action currents.

CLINICAL NEUROLOGY

In clinical neurology no important new syndrome has been described in the period under review.

Extrusion of nucleus pulposus of intervertebral discs

Love has extended his description of the symptoms of extrusion of the nucleus pulposus of an intervertebral disc to cover the cases in which the lesion is in the cervical region and the extruded matter by displacement of the theca causes pressure on the spinal cord. This gives rise to the gradual development of spastic weakness in three or perhaps in all four limbs, with no appreciable sensory loss, but often with a zone of hyperalgesia corresponding to the sensory disturbance of the spinal segment or two segments above the lesion. The symptoms typically appear a few months after an accident in which the patient has appeared to suffer little or no injury, and the sudden pain which, with similar lesions in the lumbar region, usually occurs at the time of the injury may be absent or be represented by a slight pain at the back of the neck or across the shoulders. When the patient comes for investigation there is, as a rule, no radiological evidence of vertebral injury; the spinal fluid may show merely slight increase of its protein and it is only after injection of iodized oil that physical evidence of pressure on the cervical cord is obtained. Removal of the projecting mass by operation allows full and rapid recovery of the functions of the cord.

Nystagmus of the palate

The conception of the syndrome of nystagmus of the palate has been enlarged by Guillain into 'the syndrome of synchronous and rhythmic palato-

pharyngo-laryngo-oculo-diaphragmatic myoclonus'—a title which needs no elaboration. The associated lesions are characteristically in the inferior olive and are usually of a hypertrophic type.

CLINICAL PATHOLOGY

In the clinico-pathological department, to which neurology in the past has owed so much, one of the most significant contributions is the observation of mental degeneration in association with thalamic lesions, the cerebral cortex being completely or relatively intact. Smyth and Stern described six cases of glioma or sarcoma of the thalamus in which mental degeneration was a pronounced clinical feature, and subsequently Stern described a case of 'severe dementia associated with bilateral symmetrical degeneration of the thalamus'. In this last instance most of the thalamus on each side, with the exception of the ventro-lateral nuclei and the geniculate bodies, was almost entirely denuded of ganglion cells. The degenerative process was evidently selective, bilateral, and symmetrical, and Stern regarded it as a system disease. Clinically the case was one of severe dementia of rapid course in a man aged forty-one: it was accompanied by loss of the pupillary reflexes and by such signs as forced sucking and grasping movements. Stern points out that in anthropoids the portions of the thalamus corresponding to the parts degenerated in his case project on to a very large area of the cerebral cortex, and attributes the dementia to 'isolation of vast areas of the cortex on both sides from thalamic impulses'.

NUTRITION

Turning to experimental work on nutrition there are two contributions which appear to be of outstanding importance. Chick, Macrae, Martin, and Martin have observed in pigs as a result of deprivation of certain of the vitamin B fractions symptoms of a severity hitherto unrecorded from such lack. The animals were fed on a pellagra-producing diet consisting chiefly of starch and casein with suitable oil and salt additions. When this diet was supplemented by the aneurin, riboflavin, and nicotinic acid fractions, the animals still failed to thrive and growth ceased. If to this was added the filtrate fraction of Edgar and Macrae, but none of their eluate fraction, growth proceeded for a time but was checked after 4 to 6 weeks and the animals began to suffer from epileptic fits. Frequent fits were observed in all the animals concerned, and in two of the pigs to which the eluate fraction was subsequently fed the fits ceased. Other animals which received the eluate fraction but none of the filtrate suffered from a flaccid paralysis of the hind limbs. The histological findings in the central nervous system of the animals of both groups have still to be published. As far as is known this is the first occasion on which a continuing liability to fits has been produced experimentally, either by faulty diet or by other means.

ANIMAL PATHOLOGY

From animal pathology there is a very significant contribution in the work of Innes on 'swayback' in lambs. In this disease there is a demyelination of the centrum ovale of such a degree as to cause complete softening and extensive cavitation, and in less severe cases a condition similar to that seen in Schilder's disease. Innes has found that this disease in the lambs can be prevented by allowing the ewes to have minute quantities of copper during the period of gestation. This effect of the copper may be due to interaction of its salts in the body with some other substance such as lead; Innes's investigations suggest that it is not a direct effect, but in any case this work obviously provides a clue which investigation on human demyelinating diseases must follow up. Apart from the association of certain forms of demyelinating diseases in

children with infection (such as measles and vaccinia) there has hitherto been no reliable evidence regarding the aetiology of the diseases of this group, which includes disseminated sclerosis.

EPILEPSY

Research in epilepsy continues to be largely concerned with the electro-encephalogram and is therefore a study of symptoms. Gibbs, Gibbs, and Lennox have put forward their conclusions up to 1938 as follows. Epilepsy, according to them, is a 'paroxysmal cerebral dysrhythmia'. Seizures are accompanied by distinct and characteristic fluctuations in the action potentials of the brain. The rhythm which obtains during seizures is distinctive for the three main types; *grand mal* has a fast, psycho-motor attacks (psychic variants) a slow, and *petit mal* an alternating fast and slow rhythm. The pattern of the seizure record tends to be characteristic for each patient. Antecedent to these gross abnormalities the record shows a 'lack of a competent control of cerebral rhythms'. Some patients have sub-clinical seizures, not attended by subjective or objective evidence of a seizure. There is evidence that *grand mal* may be predicted many hours in advance. In some patients abnormal activity begins in one area of the cortex and spreads to involve other areas. *Petit mal* rhythms may be temporarily abolished by a rise in the carbon dioxide tension or glucose concentration of the blood.

Golla, Graham, and Walter found that the electro-encephalogram was often abnormal between seizures. The technique and application of electro-encephalography have been the subject of a critical review by Walter.

ELECTRO-ENCEPHALOGRAPHY

Abnormal discharges from diseased areas of cerebral cortex have enabled electro-encephalography to be used as a means of localizing cerebral tumours, and this application is at present the subject of critical study at various centres.

SURGERY

Neurological surgery is making trial of a new operation devised by Sjoquist for the treatment of trigeminal neuralgia. This consists of division, by means of a suitable knife, of the descending root of the trigeminal nerve where it lies just below the lateral surface of the medulla oblongata anterior to the corpus restiforme. Since the descending root is concerned with the sensations of pain and temperature and not with light touch, a successful division of it in this situation renders the corresponding side of the face insensitive to pain and temperature but leaves it sensitive to light touch and postural stimuli. The patient in consequence does not suffer from the disagreeable sensation of numbness which is produced by division of the peripheral nerve or root, and it is claimed that he is not liable to the keratitis which may follow the older operation in cases in which the first division of the trigeminal nerve is included in the section. The conception of the operation is open to criticism on various grounds but especially because of the risks of operating on the medulla, and the uncertainty of results owing to the relatively deeper positions of the roots of the second and third divisions which it is desired to divide; the root of the first division, which is rarely affected by the neuralgia, is the most superficial.

PATHOLOGY

Greenfield, in an address on the pathology of head injuries, drew attention to the remarkable effects of cerebral oedema in causing extensive or even massive

demyelination and subsequent gliosis, and in a later paper he has described oedema of comparable degree and producing comparable effects in association with cerebral tumours. In two traumatic cases there was extreme demyelination in both frontal lobes. It was not so obvious to the naked eye as that seen in Schilder's disease, but it resembled it in extent and in sparing the sub-cortical fibres. As a rule areas of the brain which had been directly bruised were completely demyelinated but in less severe degrees the myelin sheaths were thin and beaded and stained poorly. Even when the injury affected primarily more posterior parts of the brain, the area round the anterior horn of the lateral ventricle seemed particularly liable to damage or reactionary oedema. Oedema around cerebral tumours of the more rapidly growing types, such as secondary cancers and glioblastomas, gave rise to similar massive, though perhaps less intense, demyelination. The myelin in the centrum ovale stained palely and showed separation of its fibres and degenerative changes in them. In spite of this, the myelin in the large commissural and projection tracts was relatively or absolutely normal. Axones were less affected than myelin sheaths, but in the centrum ovale they showed some degenerative changes, whereas in the cortex they were relatively or absolutely normal. Greenfield attributes the changes to anoxia resulting from excess of interstitial fluid and to a less degree from venous obstruction and reduction of the capillary bed.

THERAPEUTICS

In therapeutics the greatest advance is attributable to the introduction of M & B 693, but in sodium diphenylhydantoinate we have obtained an important palliative drug for use in a more limited sphere. Both these drugs represent achievements in therapeutic research and are not merely chance findings or applications.

M & B 693

M & B 693 or (2 *p*-aminobenzenesulphonamido) pyridine, though primarily directed against streptococci and pneumococci, soon proved itself equally effective against meningococci, and neurology quickly adopted it in the treatment of meningitis due to any of these organisms.

In such conditions the results of its administration are usually dramatic. The drug requires about 24 hours to produce obvious clinical effects and even in severe cases, given adequate dosage, cure is usually complete in 72 hours. The cerebrospinal fluid is generally free from organisms in 12 to 24 hours. Fleming has shown that organisms may acquire a tolerance to the drug and has stressed the importance of giving adequate doses from the beginning. Two tablets (1 gram) given by mouth every four hours are generally regarded as a correct and effective rate of administration, but in several severe cases of meningitis I have given three tablets every four hours (9 grams in the day) for three days without untoward effects. Cyanosis is less pronounced than with sulphanilamide, but sickness is much more frequent; toxic effects on the blood producing abrupt falls in the polymorphonuclear cell count or in the red cell count are less frequent, while toxic rashes are somewhat more frequent; both M & B 693 and sulphanilamide may, in my experience, give rise to peripheral neuritis. The fatality rate in meningococcal meningitis has been reduced to less than 10 per cent and seems likely to be reduced further, and the treatment of the disease has been changed from a prolonged and difficult to a relatively simple matter. With pneumococcal meningitis which, before the introduction of this drug, was nearly always fatal, the results are almost equally good. Some reservation must be made in regard to the more chronic cases of both diseases, the results of the new therapy in such cases having been less striking, but it seems likely that in some of the cases of this kind the results have been adversely influenced by failure to give adequate doses

of the drug at the beginning of treatment. It may almost be said that the more chronic the case, the larger should be the initial dose.

Infective diseases of the central nervous system other than meningitis seem to offer little opportunity for the application of such drugs, but no doubt some other applications will be found. The effects of M & B 693 on virus infections is still very incompletely known. The introduction of this drug will influence neurology indirectly because, with its application in cases of otitis and sinusitis, cerebral abscess must become less frequent. Similar prophylaxis of cerebral abscess resulting from bronchiectasis is less likely, though some reduction in the rate may result. Another important application of the drug within our province is in the control of bladder infections in cases of spinal disease.

Sodium diphenylhydantoinate

Sodium diphenylhydantoinate (epanutin, dilantin, solantin) was introduced for the treatment of epilepsy as a result of research by Putnam and Merritt, who found that among a large number of drugs tested, this was the one that had most effect in abolishing the irregular discharges, which are a feature of the electro-encephalogram of the epileptic subject. In practice it has been found most useful for those cases in which epileptic attacks are frequent. A young man under my care who, in spite of phenobarbitone and bromide, had from four to six attacks every night, when stabilized on epanutin had only one attack in two months. The drug is given in capsules, each containing 2 grains, and common dosages are from 2 to 5 capsules in the day. In many cases it is found best to give combined phenobarbitone and epanutin treatment.

No record of treatment of a controlled series of cases has yet been published in Great Britain. In America Merritt and Putnam have recently reported the results of two years' treatment and claim that sodium diphenylhydantoinate (epanutin) was more efficacious than other therapy in 79 per cent of cases. In an earlier paper they had claimed complete cessation of *grand mal* in 58 per cent of cases, and of *petit mal* in 35 per cent. My experience so far is by no means as good as this.

Chemically the hydantoin compound is closely related to nirvanol; it is less closely related to the barbiturates, hydantoin resulting from the condensation of urea with glycollic acid, while barbituric acid, the basis of the barbiturates, results from its union with malonic acid.

Unfortunately sodium diphenylhydantoinate is more toxic than the barbiturates and toxic rashes commonly occur, as well as untoward nervous symptoms such as ataxy, tremors, and diplopia. The margin of safety between the therapeutic and toxic effects is small, but the toxic symptoms are rarely serious and with temporary withdrawal of the drug they rapidly disappear. The use of the drug is still in the experimental stage, but it is already clear that for a proportion of cases of epilepsy the hydantoin compound is as superior to phenobarbitone as phenobarbitone was to bromide.

Nicotinic acid

Recent reports on the action of nicotinic acid in pellagra are described on p. 462.

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OPHTHALMOLOGY

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Ophthalmology presents so many different aspects that in reviewing its present position it is perhaps justifiable to deal with it broadly from its medical, surgical, and optical view-points. As the details of the position are considered, however, it becomes increasingly obvious that these divisions are very arbitrary, and their components closely interrelated.

Ocular fatigue and pain in, or dependent on, the eyes have always presented a problem of difficulty, interest, and importance.

What may be classed as optical lines of approach to the treatment of such symptoms as minor degrees of astigmatism, slight extra-ocular muscle imbalance, and, more recently, varying size of image as between the two eyes, have their vogue and their successes, but all leave a large volume of failures in cure, and therefore presumably in diagnosis. Labels such as functional and neurotic do not usually help the patient very greatly, and it would seem that there is necessary a better and fuller understanding of pain, its meaning, and its cause before its treatment is undertaken. The changing outlook on vasomotor factors and the sympathetic nervous system on the one hand, and the question of fibrous-tissue inflammation as a cause of pain on the other may open up lines of action through which the numerous sufferers from 'pain in the eyes and head' will find relief. This may go beyond the speciality of the ophthalmologist, but, as the eyes are naturally suspect as the cause of the symptoms, his judgement and discretion will probably be of major importance to the patient.

Fatigue of the ocular function from industrial causes, among which must be classed flying, plays the increasing part expected from changing conditions. A great deal of research from all angles is applied to these problems as their importance is more and more realized. Invalidism involving loss of working time, quite apart from the damage to the eyes, has focused more attention on industrial injuries, their prevention, and their treatment. This has led to the production of greatly improved patterns of protective appliances and techniques not only against the flying particle, but also against harmful chemical agents. The obstructive effects of slackness and prejudice are being gradually lessened as the importance of the issues is realized. Such advances have an international application as have many of the subjects with which the international body for the Prevention of Blindness is concerned.

OPHTHALMIA NEONATORUM

Recent international reports on ophthalmia neonatorum show how strikingly its incidence and effects are reduced by the careful control of the methods of prevention, even though opinions concerning details of the best methods may vary in different countries. Where an elaborate control is attained over the doctor or midwife's handling of the mother antenatally and of the newly-born child, the incidence of ophthalmia neonatorum as a serious entity can be reduced to something approaching complete extinction.

TRACHOMA

The position of some other 'preventable' diseases is not so satisfactory. Trachoma is a problem of varying geographical importance. Education of the people of a highly trachomatized country, and improved facilities for the better treatment of the disease, are definitely showing their effects, but the whole question of the nature of the disease and the factors that control its contagion element are still far from being settled. Control of immigrants and segregation of cases in a country but little infected show how successfully such a country can limit the danger of spread of infection.

GLAUCOMA

Glaucoma is the subject of intense investigation. The factors which make for increased intra-ocular tension are still little understood, although physiological and clinical research have to some degree cleared the issue. The grosser types of raised intra-ocular tension and the factors of 'secondary' glaucoma are perhaps better sorted out than is the type of case with insidious onset and progress, with steady loss of visual field and acuity without the evidence of even transitorily raised tension. Local senile changes within the eye, arterial disease, and other operative factors are invoked as causes, but relatively little headway is made, and the very definite geographical variation in distribution of the cases, not only as between countries but in different areas of the same country, must be a factor requiring closer investigation. Until further knowledge has been obtained, the best hopes for the limitation of the effects of glaucoma must lie in the education of the public to its dangers so that cases may come under treatment as early as possible.

MYOPIA

Myopia may not blind so many eyes as glaucoma, but it nevertheless must be regarded as a condition which should always call for more than just ordering glasses for a child, even if it cannot be entirely accepted as a 'preventable disease'. The social handicap of glasses for constant use from childhood onwards, and the serious loss of visual acuity from myopic atrophy of the choroid and retina due to a severe degree of myopia, perhaps tend to be underestimated by ophthalmologists. This is no doubt due to the number of myopes seen. but the lay parent is often naturally distressed by the inability of the oculist to do more than 'just go on ordering stronger glasses every year'. Hence the wide-spread recourse to 'exercises' from which 'cure' of the myopia cannot be expected even if the advocates of such exercises claim that the treatment prevents increase in the error of refraction. The sociological viewpoint may be that the lower degrees of myopia are biological variants, and the eugenic that sterilization offers a means of checking the propagation of high myopia, but little comfort is to be obtained from such views; it seems definite that the use of the eyes during the period of rapid growth when consolidation may lag behind expansion of tissue is the problem to be met, the risk of myopia increasing in direct ratio to the degree of myopic element in the family. Whether onset and progress are mainly in the earlier school years or around puberty when school leaving-examinations are making heavy demands on the child's eyes and strength, would seem to depend on the individual concerned and on his or her growth factor, with probably less of the familial element in the later group.

PHLYCTENULAR OPHTHALMIA

The very real improvement in child health, and the application of the increased knowledge of nutritional needs and the value of sunlight and vitamins, have

resulted in a most striking and gratifying decline in phlyctenular ophthalmia generally, and certainly in its severer forms. Although it is not yet definitely established that the disease is a manifestation of the invasion of the body by the tubercle bacillus, the decline in its severity must be the result of raised general resistance and improved health by which the body can better deal with tubercle bacilli not yet clinically manifest. The treatment of infected tonsils and adenoids has helped, with the happy result that far fewer children are having their earlier days marred by long periods of invalidism from inflamed eyes, and that fewer still will reach adult life with permanently scarred corneae, which are always liable to give rise to trouble and grossly affect visual acuity.

INTERSTITIAL KERATITIS

To some extent the same applies to interstitial keratitis. Whether because as a whole the manifestations of syphilis have lessened in intensity, or because of better treatment, this lesion of congenital syphilis is, in most cases, much less severe than as recently perhaps as 20 years ago. As both eyes are involved usually in childhood, the same relief from long-continued ocular inflammation and the same limitation of permanent corneal damage are now experienced as in the case of phlyctenular ophthalmia.

Since both these conditions may be classed as 'preventable diseases' a claim can be made that great progress has been achieved towards alleviation, which goes some way towards prevention and extinction.

MUCO-PURULENT CONJUNCTIVITIS

The wide-spread epidemics among children of freely-discharging types of muco-purulent conjunctivitis, due to the Koch-Weeks bacillus, have virtually disappeared from London, and apparently elsewhere also. The organism is seldom seen now, but seemingly in its place there is much more frequently infection by the pneumococcus. This affects both children and adults and must be regarded as a more serious infection of the eye, although perhaps its far less contagious nature and its tendency to remain uni-ocular adjust the balance. What may be the cause of these very striking changes is hard even to guess at, but the effects combined with the lowered severity of some forms of corneal disease are very apparent in ophthalmic clinics. Increasing demands are made on the refraction departments for the correction of small errors of refraction, while whole new departments are employing physiotherapy in the form of ultra-violet light and short-wave therapy, and the surgeon deals with new and varied operations in which electrical methods play a large part.

RETINAL DETACHMENT

Surgically the great advance of recent years has been in the treatment of retinal detachment. As the result of increasing attention to the sifting and analysis of types of detachment, steady advance has been made in the assessment of cases both from the aetiological and treatment standpoints. With the establishment of the fact that closure of the hole in the retina is the essential factor for successful surgical treatment, experimentation—now almost entirely by electrical means—has evolved highly successful, even if different, methods of effective closure. Patience and accuracy in localization of the hole steadily reduce the number of inoperable cases, and, whereas ten years ago any case of retinal detachment was regarded as 'almost hopeless', to-day general health conditions perhaps more than the local state preclude operation in any detachment not caused by an intra-ocular neoplasm or gross internal derangement of the eye.

Increasingly fewer long-standing detachments and grossly torn retinae are

immediately classed as unsuitable for operation. The repercussions of these changes are considerable as, apart from demanding from the ophthalmologist increased knowledge of matters electrical, the time taken in elaborate examinations and intricate operations is no light matter, and would seem, as in other branches of surgery, to create the demand for 'a speciality within a speciality'.

CORNEAL GRAFTING

The grafting of a portion of a transparent human cornea into opaque corneal tissue is now long past its early experimental stages, and the difficulty of obtaining sufficient donor material is being met in various ways, particularly by employing corneal tissue from still-born infants. Moreover, the wastage element is to a large extent obviated by making a donor eye serve for more than one opaque cornea. The details of surgical technique in this, as in more established ophthalmic operations such as cataract extraction, are constantly the subject of experiment, and fuller use of local anaesthetics to the extent of akinesia is being made in ophthalmic, as in general, surgery.

CONTACT LENSES

The most purely optical advance has been in the use of contact lenses (see p. 132).

ORTHOPTIC TREATMENT OF SQUINT

The orthoptic treatment of squint is again more than an optical matter. The value of the treatment is beyond question, but its final position in eye therapy is not yet settled. The earlier hopes that it was all that was needed for squint cases are not being realized; dispassionate research is resulting in more than the elaboration of technique and appliances, for it is enabling ophthalmologists to view the subject in its true perspective.

All these changes of ophthalmology have meant a reorientation of outlook and practice, and a widening of what was already a subject with many very diverse aspects. The established specialist must adapt himself to them. His students will realize that many of the text-book subjects now require far fewer pages than those allotted to them, and that the few lines given to newer matters must be supplemented by a great deal of new clinical information.

CONTACT LENSES

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DEFINITION

Contact lenses are thin shells of glass or other transparent material which are worn in the conjunctival sac, and cover the eyeball. They are used to correct errors of refraction and for certain therapeutic purposes.

HISTORICAL

Although contact lenses are regarded as a modern development of ophthalmology, their origin goes back as far as 1801 when Thomas Young made his hydrodiascope. This consisted of a short tube, closed at one end by a lens and filled with water. The edges of the open end were smoothed off with wax and applied to the eye. Nothing further was done until 1887 when Saemisch had a patient in whom removal of the lid for malignant disease had left an exposed cornea. This was covered with a blown glass shell, made by Müller of Wiesbaden, which the patient wore with comfort and preservation of corneal transparency until his death 21 years later. From this beginning, developments occurred on various lines and in 1911 Messrs. Zeiss produced the first ground contact lens. This was made in various sizes with differing radii of curvature for the portions designed to cover respectively the sclera and the cornea. The lens itself was comparatively small, the scleral rim being only about 4 mm. wide. Before application it was filled with physiological saline and it was then inserted into the conjunctival sac. By having a large number of lenses of different radii of curvature it was possible to obtain an approximate fit and in a few cases these lenses were worn with comfort.

In the majority, however, this was not possible because the scleral portion of the eyeball is usually not spherical. Hence the lens was not uniformly supported, bearing much more hardly on some points than on others with resulting pain and discomfort. This difficulty was overcome by Dallos working in Budapest from 1928 onwards. He employed much larger shells than the Zeiss type and aimed at using practically the whole of the bulbar conjunctiva for supporting the lens. This meant that the inner surface of the scleral portion of the shell should be an exact replica of the underlying tissue, while the inner surface of the corneal portion was ground to a spherical curve, so arranged that, when the lens was in situ, it exercised the lightest possible touch on the cornea.

OPTICS OF CONTACT LENSES

Since astigmatism is almost entirely due to error in curvature of the cornea, it can be neutralized by converting the anterior surface of this membrane from an aspherical into a spherical surface, and this is what happens when a contact lens containing physiological saline is placed on the eye. The saline fills up the irregularities of the corneal surface and, since the index of refraction of the saline does not differ materially from that of the cornea, the astigmatism of the latter is abolished. For this reason it is not necessary to grind any cylindrical correction on to the contact lens. It is also possible to correct myopia and

hypermetropia by an afocal lens (i.e. one whose anterior and posterior surfaces are concentric). Assume that the mean radius of curvature of the patient's cornea is 8 mm., and that a contact lens of corneal radius 9 mm. is filled with saline and placed on the eye. The effect will be to diminish the refracting power of the latter and so to neutralize a certain degree of myopia or, if the eye is hypermetropic, to increase the amount of error because the focal length of the eye has been increased and the image of a distant object pushed further back. A curve showing the optical effect of different radii of curvature of the corneal portion of contact lenses has been prepared by Messrs. Zeiss, from which it is possible to calculate in any given case what corneal radius will be required in the contact lens to render the patient emmetropic. The radius of curvature of the patient's own cornea as well as his error of refraction must be known.

This method was used to a considerable extent some years ago, but it had the drawback that in most cases there was of necessity a considerable difference between the curvatures of the posterior surface of the contact glass and of the anterior surface of the patient's cornea. Consequently a satisfactory fit could not be obtained, and discomfort ensued when the glass was worn. The usual procedure now is to grind the inner surface of the contact glass to a curve which will allow of its fitting the cornea, and to grind the outer surface to whatever curve is necessary to produce the required dioptric effect.

Another technique in the manufacture of contact lenses is to use blown shells, as has been done since 1888 by Müller of Wiesbaden. A certain number of successful results have been achieved, but the method is haphazard and as many as fifty shells may have to be blown before one is produced which combines an approximate scleral fit with a suitable optical correction. A recent development of this method is to blow the scleral portion of the contact lens into a mould and to grind the corneal portion as a lens of known power.

INDICATIONS

Indications for the use of contact lenses can be considered under three headings.

Optical

Any surface irregularity of the pupillary area of the cornea may produce gross interference with vision which is irremediable with ordinary glasses but markedly improved when the irregularities are filled in by the physiological saline separating the anterior surface of the cornea from the posterior surface of the contact lens. Examples of this condition include conical cornea, corneal facets, old mustard gas burns, and corneal pemphigus. High myopia is also an optical indication because in this condition a contact lens produces a larger retinal image than does an ordinary spectacle lens. A highly concave contact lens ($-30D$) may also be used as part of a telescopic combination in cases of poor visual acuity due to central retinal disease. Since contact lenses move with the eye, they can be employed in cases of high anisometropia—e.g. uni-ocular aphakia—to secure binocular vision.

Occupational

Those callings in which fogging by rain or steam precludes the use of ordinary spectacles can be satisfactorily followed when the patient is wearing contact lenses since these are kept clear by the movements of the lids.

Cosmetic

Since contact lenses are invisible and can be made of sufficient power to correct any error of refraction, they are of value to patients who wish to see clearly and yet do not wish to appear to be wearing glasses.

INSERTION OF LENSES

The finished lenses are inserted without the use of cocaine. A few drops of physiological saline are first put into the shell which is held between the fingers and thumb of one hand while those of the other hand are used to retract the lids. After a little practice and instruction, the majority of patients find no difficulty in inserting the lenses.

Toleration varies considerably and improves with practice. In a survey of patients who had had contact lenses for periods of 3 months or longer, it was found that in 18 cases of myopia there were 11 who were able to wear their lenses for periods of 6 hours or longer. In 10 cases of conical cornea all wore their contact lenses for periods of 4 hours or more and 4 for more than 10 hours a day. In 7 gas-burn cases, 5 wore their lenses for 10 hours a day or longer and in 3 cases of pemphigus one wore his lens for 12 hours a day, a second all day until re-infection occurred, and a third wore it day and night. This patient's comment, 'before having lenses I could only see forms and shadows and now I can see the headings of the newspapers', is sufficient indication of the value of contact lenses in pemphigus.

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ACUTE RHEUMATISM

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Expert mountaineers are careful to establish a series of camps, and to make good their preparations and reconnaissances before a final attempt on a fresh peak. Rheumatism and its problems require a similar approach. Wide-spread interest in the subject has stimulated such extensive research into all its aspects that we are almost prepared for the final assault. It is at this juncture that a review of the stages reached in the various researches is valuable, particularly in pointing in which direction the path lies in the future.

CLASSIFICATION

The classification of rheumatic disease has always been a difficult problem, as anyone who has attended an International Congress can testify. The pooling of ideas has been definitely retarded by the different conceptions existing in various countries. Until recently rheumatism, in the eyes of the average Continental practitioner, meant arthritis in some form or other, and there was generally a rather hazy differentiation between types of polyarthritis which might lead to cardiac involvement and those in which this danger did not exist. The French, it is true, separated off quite clearly *la maladie de Bouillaud*, corresponding to our 'juvenile rheumatism', and thereby closed the door quite firmly on any doubts as to the possible relationship of acute cardiac to chronic arthritic rheumatism. The Soviet Republic has been particularly interested in industrial rheumatism and has made great efforts to lower its incidence and improve its treatment. England and the U.S.A. have concentrated very largely on the problem of juvenile rheumatism but have also turned their attention to the more chronic forms in adults.

RELATIONSHIP OF RHEUMATIC DISEASES

There seems to be a general move towards a search for some common relationship between acute rheumatism and rheumatoid arthritis, although these are still rightly regarded as quite separate clinical entities.

A great deal of suggestive evidence has been collected from various sources, and in Germany and the Scandinavian countries there seems to be a definite view that one type of rheumatoid arthritis is a direct sequel to rheumatic fever. This is termed 'secondary' chronic polyarthritis as opposed to the 'primary' form which develops spontaneously. Such a course of events, and the reverse sequence which also occurs, make the association of rheumatic fever and rheumatoid arthritis more than a coincidence. I can recall one young girl with rheumatoid arthritis who later developed chorea and transient carditis. In another patient, an elderly woman, the two types of rheumatism seemed to alternate. During childhood she had rheumatic fever and developed mitral stenosis; this was followed by severe rheumatoid arthritis in adult life, and finally at a late age, six weeks after an acute tonsillitis, pericarditis supervened and numerous typical rheumatic nodules appeared. Acute

infections of the upper respiratory tract are known frequently to precipitate an attack of rheumatic fever, and the same may happen, though less frequently, in rheumatoid arthritis.

It is generally recognized that cases exist which are half-way between rheumatic fever and rheumatoid arthritis. A tendency for one or other of these two varieties to occur in different members of the same family has also been pointed out (Coates).

Rheumatoid arthritis in childhood is uncommon and when it does occur it tends to take the more acute form described by Still. This disease is sometimes associated with a chronic and insidious form of non-purulent pericarditis bearing a slight resemblance to that encountered in rheumatic fever. Acute rheumatic carditis is occasionally complicated by a very persistent torticollis, unassociated with cervical glands and indistinguishable from that encountered in adult fibrositis.

Poynton has drawn attention to cases of acute rheumatic fever and acute rheumatoid arthritis in which there is evidence of hyperthyroidism. Subcutaneous nodules can occur in both types of rheumatism, though their clinical behaviour and histological picture show some variations. They are practically unknown in any other human diseases. Nodules are relatively frequent in children with rheumatoid arthritis, and I have observed them in four out of sixteen cases which have come under my care during the last five years. Finally, the latest bacteriological researches point to a possible common factor.

It is not suggested that rheumatoid arthritis is a variation of rheumatic fever, but that these conditions may be closely associated as regards their aetiology. Much may be learnt from border-line cases and, especially, from a study of examples of acute and chronic rheumatism which exhibit features generally strictly confined to one or other variety.

SYMPTOMATOLOGY

Acute rheumatism is mostly seen in children, and could be satisfactorily described as juvenile rheumatism but for the fact that it may occur in adults. It has a composite clinical picture: arthritis, carditis, chorea, nodules, and erythema circinatum (the 'rheumatic state' of Cheadle). Some doubt has recently been cast on the accuracy of including all cases of 'growing pains' and chorea under the heading of juvenile rheumatism. Many vague pains in the limbs are probably the result of postural defects and debility. The low incidence of cardiac complications in several series of such cases supports this somewhat revolutionary idea (Sheldon; Hawksley).

Most authorities still regard chorea as essentially rheumatic, particularly as, even after repeated attacks, no clinical means exists of separating cases of chorea which are liable to carditis from those which are not. Nevertheless, statistics have shown that on the whole chorea is less likely to lead to heart disease than rheumatic fever and acute arthritis. Moreover, unlike other acute rheumatic manifestations, the severest examples of chorea may proceed without any increase in the sedimentation rate of the blood.

AETIOLOGY

Researches into the cause of acute rheumatism have now taken two divergent paths which it is hoped may yet lead to the ultimate solution of the problem. At the moment both theories have encountered unexpected difficulties which are so obscure and complicated that they are certainly less convincing than the early simple explanation of bacterial infection postulated by Poynton and others. A *haemolytic streptococcus* with a peculiar reaction on the part of the rheumatic subject is the basis of one view. A *virus* probably acting in conjunction with a streptococcal infection is the alternative suggestion.

Streptococcal hypothesis

It is now well established that an acute rheumatic attack can generally be divided into three phases: (1) a haemolytic streptococcal throat infection, usually mild in character and short in duration; (2) a *silent period* of two or three weeks; and (3) rheumatic fever, often with carditis of considerable severity. The clinical picture of this last phase may vary from the mildest manifestations (miniature rheumatic fever) to the gravest form of pericarditis in a fulminating attack which rapidly proves fatal. Phase 3 may be monocyclic, terminating in quick recovery or death of the patient. It may, on the other hand, be polycyclic with recrudescence of active rheumatism and relatively short periods of improvement; or again phase 3 may be prolonged indefinitely in an active 'rheumatic state' with gradual deterioration or ultimate recovery of the patient's health. Immunity responses to the foregoing streptococcal infections have been investigated by the author and his colleagues at the Hospital for Sick Children, Great Ormond Street, throughout the stages leading to the acute attack.

Coburn also has devoted the last few years to an intensive study of this problem and has been able to demonstrate that a delayed antibody-response in the formation of antistreptolysin on the part of the patient is associated with a rheumatic relapse. He suggests that a rheumatic attack or relapse results through the patient being unable to eliminate the products of haemolytic streptococci promptly from the system, but the explanation is not entirely convincing. It is particularly puzzling, for instance, to find that rheumatic subjects who escape any ill-effects of a streptococcal throat infection sometimes produce *no antibody (antistreptolysin) response at all*, although as a rule their reaction is a prompt one.

Serological studies are certainly a most difficult and complicated problem; this applies even more to the interpretation of any results obtained. Coburn and Pauli's latest discovery is a good illustration. They found that the serum of a rheumatic patient taken during phase 2 of an attack precipitates the serum of the same patient taken during phase 3. The same reaction could be demonstrated with the sera of different rheumatic patients, provided the blood was collected at the appropriate times. The nature of the precipitogen is unknown and, in this instance, appears not to be related to the common streptococcal antigens.

Virus hypothesis

After being launched with great hopes, the hypothesis of a possible virus as the cause of acute rheumatism (Schlesinger, Signey, and Amies) no longer appears to be so simple. The presence of particles resembling elementary bodies in acute rheumatic exudates has been confirmed (Eagles, Evans, Fisher, and Keith), but similar bodies were also demonstrated in the joint fluids of patients with rheumatoid arthritis. Cross-agglutination experiments were successfully carried out with material obtained from rheumatic and rheumatoid sources. This may be another point in favour of a possible relationship of these two types of rheumatism.

Further researches on the virus have, however, somewhat weakened the original claim put forward, since it has been shown that suspensions of 'elementary bodies' obtained from strictly rheumatic sources could be agglutinated with the sera of patients with quite unrelated arthropathies (Eagles and Bradley). The natural deduction is that the virus is either much more widely distributed in man than is generally supposed, or that particles seen in the suspensions are not true virus bodies at all. Attempts to reproduce acute rheumatism in animals by injecting the 'virus' in various ways have proved unsuccessful, although isolated examples of valvulitis have resulted (Schlesinger and Signey), and one or two sudden deaths have been reported

with cardiac failure and severe myocarditis (Eagles *et al.*; Dyson). Fibrositis has also been induced in rabbits by the intravenous injection of a virus together with a haemolytic streptococcus in doses which proved harmless to the animal when either of these two infective agents was injected alone. The virus, however, in these experiments was obtained from a non-rheumatic source, its virulence having been artificially raised by passage through living animal tissues (Gordon).

Finally, Homer Swift, until recently a staunch adherent of the streptococcal hypothesis, in conjunction with Brown, reported the isolation of a 'pleuro-pneumonia-like' virus from human rheumatic exudates, which was pathogenic to laboratory animals. With this 'virus' lesions were produced in the chorio-allantoic membranes of chicken embryos, and the experiment could be repeated after as many as twenty-four serial passages. It was not decided whether or not the infective agent was a true virus or a filtrable stage of streptococcal growth.

As in the case of the streptococcus in acute rheumatism, the virus hypothesis has thus reached the same inconclusive stage. Failure to reproduce the disease experimentally is, however, not conclusive evidence against either theory. Rheumatism is not a natural disease in any laboratory animal, and failure to reproduce certain other human infections in animals has also been encountered, for example, scarlet fever, chicken-pox, and herpes zoster.

PATHOLOGY

A good deal of histological work has been done during the last few years on the subcutaneous rheumatic nodule and the corresponding microscopic Aschoff node in the heart. Three main stages are now recognized in these vascular connective-tissue lesions: (1) oedematous swelling of the collagen fibres, with deposition of fibrin in small necrotic areas; (2) vascular damage, with infiltration of white cells from the circulation and proliferation of the fixed tissue cells (appearance of large mononuclear and giant cells); and (3) organization and fibrous tissue replacement, with final regression of the lesion. In fulminating carditis the myocardial inflammatory changes may hardly have passed beyond the first change when death occurs; this would account for the absence of typical Aschoff nodes in such cases.

It is surprising how quickly and completely a subcutaneous rheumatic nodule may disappear leaving no trace of its former existence. In some cases the myocardium recovers to the same degree, but more often slight or severe permanent damage remains. The valves seem to be particularly vulnerable, cicatrization and deformity being the common sequelae of rheumatic inflammation in this region.

There has been some argument whether the node or nodule just described is a granuloma confined to rheumatic infection or whether it may not just be an allergic tissue-reaction to certain foreign proteins mostly of bacterial origin. Experiments have been described in which an attempt was made to reproduce Aschoff's nodes and subcutaneous nodules by injections of horse serum (Klinge) or human blood (Mote, Massell, and Jones) respectively, but the results recorded were not very convincing, and have not been confirmed.

Proliferation of large mononuclear and giant cells in a rheumatic nodule is probably a phagocytic response to the rheumatic infection. Micro-organisms have never been satisfactorily demonstrated in such lesions, but special staining of the cells by Mann's method suggests the presence of inclusion bodies, possibly derived from a virus infection.

A most interesting recent line of investigation has been the study of the morbid anatomy of fatal cases of rheumatic carditis and its correlation with the physical signs noted during life (Bland, Duckett Jones, and White). It

was clearly demonstrated that in a considerable number of cases (69 per cent) in which apical diastolic murmurs had been audible and mitral stenosis presumed, there was no anatomical narrowing of the mitral orifice whatever. Gross deformity and scarring of the mitral orifice without real stenosis were present in a certain proportion, but in a far greater number damage to the mitral valve was minimal. Diastolic apical murmurs of the Austin Flint variety could be excluded in all save two cases, in which disease of the aortic valve was also present. This discovery may upset the current teaching on the significance of murmurs, but it is not very surprising, and has long been suspected by those who have had the care of large numbers of rheumatic children.

The cases just mentioned were all fatal, mostly from a recrudescence of rheumatic carditis. Fortunately this is not the inevitable course of the disease, and the results of the investigation should influence the general tendency to diagnose mitral stenosis too frequently, thereby rendering the prognosis less favourable.

We have been taught to regard mid-diastolic murmurs at the apex in rheumatic children as evidence of early mitral stenosis. It is now known that these may ultimately disappear in the course of years as the patient recovers. Evidently the diagnostic criteria of early mitral stenosis require revision.

PROGNOSIS

It is now generally known that a smouldering rheumatic infection may take many months to subside, and that there is more likelihood of recovery occurring in special country convalescent hospitals provided for the purpose. The Invalid Children's Aid Association has for long been the pioneer in such schemes. Municipal authorities in various parts of the country are now gradually shouldering the responsibility and are making suitable arrangements for dealing with the problem in their particular areas. The London County Council is now spending about £220,000 annually for the purpose. In June 1937 they had on their register over 20,000 rheumatic children, 8,500 of whom were receiving treatment at that time. The Council has to deal with as many as 2,000 applications for admission to special units per annum (Thornton).

Prolonged convalescence in special country homes has now been in existence long enough to offer some idea of its ultimate effect on the prognosis. In the author's experience this is certainly more hopeful than was generally believed in the past, and similar reports have been published in America (Bland, Jones, and White).

One of the criticisms often levelled at the system of special convalescent homes is the risk of upper respiratory infections spreading through a community known to be particularly susceptible to them. This risk has not been overrated, and its dire effect on the rheumatic child has been the subject of numerous communications. Unless proper precautions are taken, convalescence in these homes will certainly defeat its own object, and may do more harm than good. Medical authorities in charge of these institutions should therefore make routine arrangements for isolating cases in this emergency, and the nursing staff must be alive to its dangers. Space and ventilation are very important considerations in such institutions, and overcrowding must be carefully avoided.

TREATMENT

Prevention

This is always the ultimate aim in every disease, but is difficult to achieve when the cause of the infection is undetermined. Certain predisposing factors

have, however, been sufficiently well established to suggest measures to counteract them. Overcrowding, bad housing, protein and vitamin deficiencies in the diet, clothing defects, and lack of proper holidays are probably the combined factors responsible for the greater prevalence of rheumatism among the poor. Poynton stresses the deleterious effect of damp cold. All these effects are largely the penalty of urbanization, which lowers the vitality of the young, acts adversely on their nervous temperament, and increases the chances and dangers of droplet infection. At the same time dwellings in some country districts may be very poor.

Prevention under these circumstances is no easy matter, but much may be secured by individual effort in conjunction with school medical officers, rheumatism clinics, and special convalescent hospitals. Leicester is one of the most recent cities to embark on a scheme of this nature, and Braithwaite has been able to show how important it is to devote attention to every possible factor. It is significant that as the poorer section of the community in Leicester moved out to the new housing estates, so juvenile rheumatism has moved with it. The provision of better housing with an improved 'microclimate' was obviously not sufficient to reduce the incidence of the disease, as other factors were probably made worse by the move into new estates. For example, the rents were higher, and a larger proportion of the family income had to be spent on fares, with a corresponding deterioration in the quality of food. Distances to school were greater, and the children were thus more exposed to bad weather and fatigue.

Municipal campaigns attempting to improve the social existence of school children are very necessary, but should be undertaken with a broad view. Advice to the mother may be very useful, but this has often to be supplemented by practical assistance as well as by the provision of better dwellings. Facilities for convalescence in the case of debilitated children are most valuable, and will certainly help to increase their general resistance.

Examination of all children leaving fever hospitals, especially patients recovering from scarlet fever and diphtheria, as is carried out by Sheldon in Walthamstow, may single out an appreciable number at the very onset of their rheumatic infection. Proper treatment can then be given at once and such cases can often be prevented from becoming serious.

Curative

There exists as yet no specific form of therapy for the acute or active stages of rheumatism. Sulphanilamide, that panacea for so many infections, has proved valueless and even detrimental, a fact which must give food for thought to those who strongly uphold a streptococcus as the infective agent.

Acute throat infections in rheumatic children should be vigorously treated, as there is still a chance during 'the silent period' of preventing or controlling a relapse. It is therefore rational to give a course of sulphanilamide when tonsillitis occurs, although there is no evidence that it is any more effective given in this way than aspirin. Until there is further advance in our knowledge concentrated aspirin therapy is the best prophylactic measure for rheumatic children who contract throat infections. Without careful supervision, however, many of these attacks are bound to be missed as they may be very mild.

Rest still remains the best form of treatment, but it must be given with a strict eye on the patient's rheumatic state, continued as long as this is active, and gradually relaxed as it becomes quiescent. The weight, temperature, and pulse-charts constitute a guide to the course the disease is taking, while the physical signs in the heart, the blood sedimentation-rate, and possibly the electrocardiograph provide the additional evidence required. It is hardly necessary to add that the presence of nodules, chorea, or a rheumatic rash is obvious evidence of active disease.

In conclusion we might add that the future holds great hope for the final

solution of the problem of acute rheumatism. Not only are we on the eve of great discoveries regarding the cause, but at last practical steps are being taken to treat the disease at an earlier stage, and, what is even more important, to find means of preventing it altogether.

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TROPICAL MEDICINE

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The remarkable advances in tropical medicine during recent decades are largely due to biological researches in relation to the insect carriers of malaria and other diseases. The time is long past when an expedition to the tropics of a few months' duration could make important additions to knowledge of some little investigated disease, but prolonged team work on biological lines is steadily adding to the methods of prevention against some of the most widespread and serious of tropical diseases. Equally important is the complementary work of chemotherapy in providing more new curative remedies in the last four decades than had resulted from empirical methods during many previous centuries, important as the latter have been in the case of malaria and amoebiasis. The improved treatments of amoebiasis and leprosy are also due to therapeutic investigation on modern lines of comparatively inefficient empirical drugs. Advances in the knowledge of hormones and vitamins have already proved of great value in the treatment of sprue, beri-beri, and pellagra. A résumé of recent advances on these various lines will thus serve to illustrate the present trend and future prospects of tropical medicine.

MALARIA

Malaria, the most wide-spread disease in the world, remains the greatest problem in medicine. This disease has recently been estimated to be responsible, directly or indirectly, for two million deaths and an economic loss of 67½ million pounds yearly in India alone.

Biological prophylaxis

When, four decades ago, Ronald Ross proved malarial infection to be carried by mosquitoes, it was naturally hoped that the disease might be controlled by destroying the larval stage of the incriminated insects which takes place in pools of water. This hope was at first sight strengthened when the Royal Society's workers found that only certain varieties of *Anopheles* are efficient carriers of malaria. But subsequent investigations have only revealed increasing difficulties in the discovery and destruction of the carriers owing to every country presenting different local problems, as the following recent examples show.

A. culicifacies is the main carrier of malaria in large areas of India and was responsible for the Ceylon epidemic of malaria in 1934-35. Yet in Bengal the local conditions are unfavourable to its efficiency as a carrier. In Malaya sub-soil drainage proves a valuable prophylactic measure, but in Assam it proved a failure, or even made matters worse, owing to the heavier rainfall in a flat country with insufficient fall for drainage. The *A. minimus* carrier in Assam and elsewhere can be controlled by planting vegetation affording shade along the small streams in which it breeds, but in more hilly country intermittent flushing of the streams gives better results. Thus a method that gives good results in one country may be inefficient against the same anopheles in another area, so that each presents a local problem for solution by experts in malaria.

Still more complicated are conditions under which malaria is spread by the same species of anopheles in different countries of Europe, for the Rockefeller Foundation's investigators showed that indistinguishable adult insects may be good carriers in one area but very poor ones in another. The explanation was found in the fact that some varieties of this carrier are distinguishable from each other only by microscopical differences in the egg floats they lay on water. Thus, in Holland, examination of thousands of anopheles in human habitations showed that *A. maculipennis atroparvus* was naturally infected with malarial parasites 118 times as often as *A. maculipennis messeae*. Yet these two varieties were only distinguishable by the size of their salivary glands and the structure of egg floats—so minute are the biological variations which are of the greatest practical importance in the prevention of malaria. In Holland also differences in the size of the salivary glands served to distinguish a type of *maculipennis*, with great infective powers, breeding in saline water and wintering in the houses of the people, from a harmless form breeding in fresh water and hibernating in cool places away from the warmed houses during the cold season. This observation explained the high malarial incidence in north Holland with saline waters, and the low prevalence in south Holland with the harmless fresh-water breeding form. The reclamation of land from the sea in north Holland may thus in time reduce malaria there. Through such biological researches the malarial problems and methods of prevention are steadily being worked out in different countries.

The fact that malaria is known to have died out in extensive areas of Europe without the elimination of anopheles is an encouraging sign. Rotation of crops, and other improvements in agricultural methods, have helped in this process, and these methods have already proved of great value in Italy.

Prophylactic measures other than the destruction of anopheline larvae are continued for the most part on well-tried lines. In European countries increased attention is being paid to killing anopheline carriers in the houses of the people by fumigation and spraying. In India barracks have been dealt with by combined fumigation and trapping of the escaping insects in large muslin bags fixed outside the only open portion of a window, towards which they fly. In Natal and Zululand large-scale weekly spraying with pyrethrum preparations has greatly reduced malaria after the failure of larvicides and of quinine distribution.

Immunity and premunition

It is now generally recognized that the material reduction of malaria by control of anopheline species, directed against the local carriers by the methods above dealt with, is impracticable on the score of expense in extensive rural tropical areas with a poor population. Where large expenditure is possible, as during the construction of the Panama Canal, and as a commercial proposition on some rubber and tea estates, success may be obtained such as is not feasible in large hyperendemic malarious areas of tropical Africa and parts of India, where few escape malarial infection. In such countries all the very young children become infected, with considerable mortality, but those who survive cease to suffer materially from the disease. In many such, a mild latent infection persists and protects against further serious infection. This is known as premunition, and immunity only persists as long as a slight degree of infection remains. Complete cure may render such persons liable to reinfection, in much the same way as in syphilis. In birds malaria produces lasting premunition, but in mankind repeated infections are required, as is seen in artificial malarial infections with a particular strain of malarial parasite in the treatment of general paralysis of the insane. It has therefore been suggested that in hyperendemic areas it may not be advisable completely to cure malarial infections.

Some species of monkeys show great resistance to malarial infection, but

this can be broken down by splenectomy. This is explained by the observation that monkey immunity depends on the rapidity with which the macrophages of the reticulo-endothelial system can phagocytose infected red corpuscles, a process that is greatly increased during acquired immunity. Much light is thrown by such experiments on the problems of human malaria.

Chemotherapy in malaria

In the vast malarious areas in which prevention on biological lines is impracticable for various reasons, reliance must be placed on treatment for the mitigation of the ravages of the disease. Invaluable as quinine and other cinchona derivatives have proved during the last three centuries, their action is deficient in at least two important respects. In the first place the rapid control of the febrile attacks is too often not curative, as is shown by the frequency of relapses. Secondly, quinine has no lethal action on the gametocyte stage of the malarial parasites, through the development of which in anopheles the infection is spread. Moreover, quinine is far too expensive for general use among the vast number of poor people stricken with malaria in tropical countries, although this is to some extent being remedied by the use of the cheaper total alkaloids of cinchona bark in the forms of totaquina and the Indian-made cinchona febrifuge, which are equally effective.

In recent years chemotherapy has come to the rescue by providing variations in the structure of antimalarial drugs, the efficacy of which is tested against the malarial infections of birds and monkeys. The most effective remedies yet provided by these discoveries are atebirin and plasmoquine, the actions of which are complementary to each other. Atebrin is as effective as quinine in controlling the febrile attacks, and in smaller doses in making the treatment slightly less costly. Relapses also appear to be somewhat less frequent, although atebirin still leaves much to be desired in that respect, so that the ideal drug remains to be found. Plasmoquine in small non-toxic doses is much less effective against the febrile symptoms, but it possesses the invaluable quality, not found in the two other drugs, of destroying the mosquito-infective gametocyte stage of the parasites, and thus rendering the patient no longer infective to others through anopheline bites. For example, by treating all the occupants of tea-estate coolie lines, not omitting the highly infective children, at the beginning of the fever season, the seasonal incidence of malarious fevers has in some instances been greatly reduced. Equally important is the administration of small doses of plasmoquine subsequently to quinine or atebirin; this so greatly reduces the relapse rate that, among the British troops in India, the yearly number of malarial attacks per annum has been reduced to about one-third of the former rate.

Drug prophylaxis

The therapeutic use of induced malaria in certain mental diseases under experimental conditions has thrown unexpected light on some aspects of human malaria. The most important was the discovery that prophylactic doses of quinine are only effective against the injection of infected blood, but not against the mosquito-induced disease. This led to the suggestion that the sporozoites injected by infected mosquitoes undergo a previously unsuspected further cycle of development in the reticulo-endothelial system of the spleen and other tissues before they can develop in the red corpuscles and produce clinical malaria susceptible to quinine. Such development has since been described in bird malaria. It follows that quinine is not a true prophylactic against mosquito-induced malarial infection; it delays for long the development of febrile attacks, but they occur when the drug is stopped. Atebrin also fails in this respect, although there is evidence that either drug combined with plasmoquine is more effective as a prophylactic.

Further chemotherapeutic studies are therefore required to furnish a cheap

and effective prophylactic drug against malarial infections. The highly encouraging progress made through post-war research on malaria affords good hope of still further progress on the above lines in future.

YELLOW FEVER

The problem of the control of yellow fever in America and in tropical Africa is also essentially biological. The rapid decline of the disease in the large cities of the West Indies and South America at the beginning of the present century resulted from anti-mosquito methods based on the discoveries of Walter Reed's Commission of 1900. The subsequent discovery of the wide-spread incidence of yellow fever in West Africa opened up a new problem owing to difficulties of mosquito destruction among the scattered population of that area. The discovery that, although West African monkeys are immune to yellow fever, those imported from India were susceptible opened up a new field of experimental research, for in the absence of that knowledge human subjects had to be used for dangerous experiments in Walter Reed's time. A great advance was made when it was established that mice could be infected intracerebrally, and that by repeated passage the virus could be so attenuated that it could safely be used for prophylactic inoculation. This in turn provided a solution of the difficult problem raised by the discovery in Brazil of the jungle form of yellow fever, which could not be controlled by mosquito destruction, but the spread of which has recently been checked by large scale preventive inoculations.

A further outcome has been the mapping out of the yellow fever infected areas of tropical Africa by the mouse protection test. This is dependent on the finding that the life-long immunity after an attack of yellow fever is due to the continued presence in a small quantity of the blood of such persons of sufficient immunizing substance to neutralize a dose of yellow fever virus lethal for a mouse. By testing the sera of a number of persons in any place for the presence of the protective substances, both the former prevalence and approximate date of a former outbreak of yellow fever can be determined; for, if only the sera of persons over twenty years of age protect mice against infection, yellow fever must have been present in the place over twenty years ago. By these means the Rockefeller investigators found that the disease occurs from tropical West Africa eastward as far as the Anglo-Egyptian Sudan, and southward through the Belgian Congo to the north of Angola. Europeans going to any part of this huge area are liable to become severely infected from the comparatively mild form prevalent among the local population but not easily detectable. Protective inoculation is therefore being performed on Europeans going to French West Africa more especially, and also on the passengers going from the endemic area to uninfected countries by aeroplane, and the planes are being disinfected as regards mosquitoes by fumigation.

Much therefore can now be done towards preventing yellow fever infections. Unfortunately no recent advance has been made in the treatment of the disease, although the serum even of long recovered cases may possibly be of some value. Chemotherapy so far has not provided any curative remedies against the common virus diseases of man and animals, and work in that direction is much to be desired.

TRYPANOSOMIASIS AND SLEEPING SICKNESS

Trypanosomiasis, with its extremely fatal sleeping sickness stage when the organism invades the cerebrospinal system, presents also mainly a biological problem of the control of infection through the tsetse-fly carriers. How serious

is the problem will be evident from the conclusion of the League of Nations Health Report on the distribution of the disease in African tropical countries with an estimated population of 65 million people; for the examination in a single year of 7 million persons revealed 140,000 fresh cases in addition to a similar number of older ones. The disease has recently spread greatly in Nigeria, where in 1939 it was reported that 300,000 cases had been treated in the previous seven years. Under epidemic conditions, such as prevailed at the beginning of this century among the crowded fisher folk on the northern Uganda shore of the great Lake Victoria Nyanza, the causal parasite was conveyed directly from the blood of one patient to another by the bites of the tsetse-flies without the occurrence of the developmental cycle of the flagellate in the fly. More usually a fly infected through biting one patient becomes infective to another only after a cyclic development of some three weeks' duration in the gut to a stage when the head parts become infected, and the insect then remains infective as long as it lives. The problem of control is greatly complicated by the fact that both cattle and wild animals serve as reservoirs from which the flies can be infected with the parasite of man. The long controversy on the danger of infection indirectly from wild animals has been elucidated recently by experiments in which the human trypanosomes have been maintained for several years in antelopes, sheep, and monkeys, and have then been proved by direct experiment to be infective to man, especially by the tests of J. F. Corson on himself—thanks to such early infections being now readily curable by the chemotherapeutic remedies mentioned later.

Various measures based on such knowledge for the protection of mankind from the bites of infected wild fly have been found of value in different areas. In South Rhodesia extensive and costly big game shooting has been relied on for years to keep in check the specially virulent form of sleeping sickness prevalent in that and some other areas. In Kenya the *Glossina palpalis* carrier seldom flies more than two hundred yards from the rivers and lake shores, so the most economical plan has been found to be to isolate two-mile blocks by clearings of the jungle, and to catch the flies in the riverine areas by squads of native boys with nets. A considerable agricultural area has been repopulated by this means. In Tanganyika, as in the case of the earlier Uganda epidemic, it has been found best to move the people to open land free from the tsetse-fly, but in the Belgian Congo movement of the people to fly-free higher areas has not been a success owing to the lower agricultural value of the new sites. In the Southern Sudan the yearly examination of all the people, and treatment of the cases in settlements, prevented sleeping sickness from becoming epidemic and depopulating the country, as it did in the absence of such measures in a neighbouring area of French Equatorial Africa. All these are instances of successful biological control.

In this disease also new chemotherapeutic remedies have proved of immense value in supplementing preventive measures. In the first stage of infection limited to the blood stream Bayer 205, or moranyl, is rapidly curative. These drugs are excreted slowly, so that a single injection of either protects against the infection for three or more months. In a severely infected Congo area repeated prophylactic doses were given to all persons with enlarged glands, and an outbreak was thus controlled. Once the cerebrospinal system has become involved, however, these substances are of comparatively little value.

Fortunately trypanamide, discovered in the Rockefeller Foundation laboratories in New York, is effective in most second- and third-stage sleeping sickness cases because it penetrates to the nervous system. By the use of trypanamide in 10,000 patients as many as 75 to 90 per cent of sleeping sickness cases have been cured in parts of the Belgian Congo and in the Cameroons. It is important to give from the beginning as full doses as possible, short of giving rise to eye trouble, for if a cure is not effected the surviving trypanosomes may become resistant to arsenical drugs.

For this reason it is important to find drugs of a different chemical constitution that will be effective in arsenic-fast cases, and much promising research is being carried on for this purpose. Warrington Yorke and his colleagues have found guanidine compounds such as synthalin to have a powerful trypanocidal action even against strains in animals resistant to Bayer 205 and tryparsamide. C. H. Browning has obtained two of a series of phenanthridine and phenanthridinium compounds curative in mice. It is on these lines that further progress is most likely to be made in the cure of trypanosomiasis.

THE TYPHUS GROUP OF FEVERS

A striking feature of recent work on tropical medicine has been the discovery of various forms of typhus fever in many parts of the world. Once more the problem is mainly biological, and is complicated on account of the number of insect vectors involved in transmission. The long known epidemic typhus of eastern Europe particularly is comparatively simple as the infection is conveyed direct from man to man through the body louse. The non-epidemic or sporadic forms differ in being primarily infections of rodents, such as rats and mice, from which the causal rickettsia bodies are conveyed to man through the bites of fleas, ticks, or mites in the different forms of the disease.

A curious feature of this group of fevers is the diagnostic value of the agglutination by the patients' blood of different strains of intestinal *Proteus* bacteria, with some overlapping in the different forms of the fever. This may be related to the occasional invasion of the human blood-stream by these organisms from the bowel in typhus cases. The areas affected by the non-epidemic typhus group are constantly being added to, and they are difficult to avoid as some of them are contracted in the jungle. A vaccine made from the live flea virus has been used, and that of wood ticks emulsified in phenol-saline is reported to have reduced the mortality of the Rocky Mountain form in the United States from 82 per cent to 6.6 per cent. This is fortunate because there is as yet no specific treatment for typhus fevers.

RELAPSING FEVERS

The relapsing fevers due to spirilla present very similar problems to those of the typhus group, for the epidemic form is louse-borne and the non-epidemic African form is conveyed by ticks which remain infective for long in native huts and rest-houses. In this group should be included rat-bite fever, of wide distribution but especially prevalent in Japan. Fortunately all three forms of spirilla fever are amenable, if taken early, to neoarsphenamine. It has also been demonstrated that the intravenous injection of this drug is followed by a great production of antibodies in the blood of mice following the destruction of the *Spirillum recurrentis* of relapsing fever. This is much less if the spleen has been previously removed.

KALA-AZAR

Kala-azar is due to a protozoal organism the flagellate stage of which was discovered in cultures in 1904. Nearly two decades, however, elapsed before extensive development of that stage, with involvement of the mouth parts, was obtained in sand-flies fed on the blood of infected patients, and several years later the Chinese hamster was occasionally infected after a very long incubation period by the bites of sand-flies infected from human cases. It is still a disputed question whether that is the sole mode of infection, for it has been found that in a number of incompletely cured patients, and occasionally after spontaneous recovery, dermal lesions that have been mistaken for leprosy nodules appear in large numbers and contain very numerous *Leishmania*

donovani organisms which have also been found in nasal and pharyngeal discharges. Moreover, the Mediterranean or infantile form of kala-azar infections has repeatedly been associated with the occurrence of the disease in dogs which also suffer from dermal infections without obvious lesions. The infection of dog ticks or of sand-flies might occur from feeding on such lesions. Moreover, animals are much more easily infected by inoculations into the skin than through sand-fly bites, so that the possibility of direct infection through contact with skin lesions is receiving increased attention.

The control of kala-azar through the destruction of the breeding places is rarely practicable, but the fumigation of houses appears to be rather more feasible. Thus three and a half decades of biological research has failed so far to furnish an effective means of controlling the incidence of kala-azar, although as early as 1896 Rogers showed that the infection in the Assam epidemic was a house or site one. His suggestion to move the healthy from infected coolie lines and villages to new sites, however, enabled the disease to be stamped out of a number of seriously infected tea estates, and the progress of the epidemic up the Brahmaputra valley to be checked for two decades.

In this case chemotherapy has furnished the means of controlling the disease through effective treatment rapidly reducing the foci of infection wherever it has been carried out on a large scale. Tartar emetic intravenously was first found in 1913 to be effective against the closely allied *Leishmania tropica* infections of Brazil and was soon shown to be curative of both the Mediterranean and the Indian forms of kala-azar after two or three months' treatment. Chemotherapeutic researches subsequently furnished more rapidly curative remedies in the form of neostibosan for intravenous, and later solustibosan for intramuscular, injection, the latter being of great advantage in young children who are so often infected. By means of these drugs some 90 per cent of typical kala-azar cases can be cured after eight days' treatment, in place of a former case mortality of over 90 per cent in the Assam epidemic cases. In fact the disease was eradicated from a group of infected villages near Calcutta by systematic seeking out and treating all the cases over a period of seven years. Great decrease of the disease has also been effected by systematic treatment by at least two mission hospitals in India, and only sufficient funds and staff are required greatly to reduce the incidence of kala-azar.

PLAGUE

The pandemic of plague that spread in 1894 from Southern China to Hong-Kong and was carried by sea to India and to every continent is still widely prevalent, although it has greatly abated in recent years, especially in India. In spite of its being a bacterial infection its control presents largely the biological problem of breaking at some point the chain of infection from rats and other rodents, through the bites of their fleas, to mankind. The establishment of the rat-flea theory of infection has furnished the means by which future epidemics may be prevented from spreading by sea from one country to another, through the use of sulphur, hydrocyanic acid, and recently the less dangerous methyl bromide fumigation for the destruction of rats and their fleas on ships.

In the absence of any efficient treatment—for even the improved Bombay serum has not yet been proved materially to reduce the death-rate—vaccines are of great value in prophylaxis during outbreaks. In India sterilized cultures of virulent organisms have proved effective, and in the Dutch East Indies and in Madagascar very favourable results have followed the use of vaccines made from living attenuated plague bacilli.

HORMONES AND VITAMINS IN THE TREATMENT
OF TROPICAL DISEASES

The importance of deficient diet in predisposing to, or causing, tropical diseases is being increasingly recognized. Of greater interest, however, are the curative measures that have resulted from advances in our knowledge of the physiological actions of the internal secretions, or hormones, and the closely allied vitamins.

Sprue

In sprue, liver soup had for long been used empirically at the London Hospital for Tropical Diseases before it was discovered in America that liver extracts contain substances that have a direct curative action in the pernicious form of anaemia, which constitutes the most dangerous feature of sprue, especially in subjects over middle age. Liver extracts orally suffice in most such cases, but intramuscular injections are more effective in the severer grades.

Beri-beri

The discovery that the vitamin B complex includes several substances has led to an important advance, for injections of pure vitamin B₁ in full doses have been followed by remarkable recoveries within a few hours from the very grave cardiac form of wet or dropsical beri-beri met with in the Straits Settlements.

Pellagra

Pellagra has for long been associated with diets in which the proteins have a low biological value, as in the case of maize. The absence of some hypothetical dietetic factor has also been postulated, and this appears to be confirmed by the recent reports of a number of cases of the disease in which great benefit accrued within 12 to 48 hours of the administration of nicotinic acid orally or by injection.

The foregoing examples will suffice to show that satisfactory progress, both prophylactically and curatively, is still being made in the field of tropical medicine, mainly through biological and chemotherapeutic researches. Full reduction of suffering and mortality now obtainable through the advances of medical science will not, however, accrue until medical administrations can supply to the village populations of Africa, China, and India a well-trained indigenous medical staff to make use of them.

UROGENITAL DISEASES, VENEREAL

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The diseases dealt with in this article are syphilis, gonorrhoea, soft chancre, granuloma venereum, balanitis gangrenosa, lymphogranuloma inguinale (poradenitis venereum or lymphopathia venereum), and waeisch (sago-grain or millet-seed) urethritis.

METHODS OF PREVENTION

The prevention of venereal diseases is usually discussed under two main headings, namely personal prophylaxis and anti-venereal measures undertaken by health authorities.

Personal prophylaxis

The controversial question of the value of personal prophylaxis remains unsettled, but probably most who have studied its results agree that it is by no means the solution of the venereal problem.

Chemical disinfection after intercourse is thought by most authorities to be valuable if carried out promptly and by a skilled attendant, but in practice it is often too much delayed to be effective.

Concerning disinfection by self-applied chemicals there is by no means such unanimity. In the British Army the prophylactic outfit is considered by some to be responsible for a great reduction in the incidence of venereal diseases, but the high rates in troops stationed abroad where venereal diseases are more rife than in Great Britain show that, for one reason or another—usually careless application—it is not a powerful anti-venereal measure. The substitution of the condom alone for condom and disinfectant in the prophylactic outfit of the Royal Navy is a significant commentary on its value.

Activities of health authorities

Prophylaxis of syphilis by arsenical chemotherapy has not gained in popularity, probably because most syphilologists fear that the drug may prevent the chancre but not the infection, and that the intelligent patient may be tortured for months or even years by dreadful uncertainty as to whether or not he has been infected.

A method of prevention which has gained some popularity in places where prostitutes are 'regulated' is to give them injections of an insoluble compound of bismuth so that their tissues may always present a bismuth barrier to invasion by *S. pallida*. In this way Sonnenberg, for example, claims to have kept prostitutes free from infection for as long as nine years.

Prevention of venereal diseases by most public health authorities consists chiefly of measures to enlighten the public on the dangers of these diseases and on their avoidance and to insure treatment of the greatest possible proportion of the infected in the community. On the principle that enlightenment

is desirable practically all are agreed. On methods of enlightenment there is wide diversity of opinion, especially as to the value of film displays and lectures to large audiences. There seems to be far greater support for instruction of the young in biology, simple physiology, and care of the body, including avoidance of disease, and for instruction of selected groups of people such as parents, nurses, group leaders, and so forth to whom young persons often turn for confidential advice.

Results of measures for treatment of the infected are mentioned below in the survey of the position in respect of the different venereal diseases.

SYPHILIS

In the article, Syphilis, in Volume XI, p. 529, it was stated that, thanks to discoveries of the causal organism, diagnostic blood tests, chemotherapy by arsphenamine and bismuth compounds and pyrogenetic therapy, this disease had become controllable to a degree probably unsurpassed in any other systemic disease. The development of the sulphonamide treatment of bacterial infections may now perhaps have made a number of other diseases more controllable, but the position remains that the eradication of syphilis from the community depends only on the proper use of existing knowledge.

Microscopical examination

Too little use is still made of microscopical tests in the diagnosis of early syphilis. It is not sufficiently appreciated by practitioners that this method is available to everyone who can fill a capillary tube with discharge made to ooze from an early lesion by scraping it, and that it can afford a certain diagnosis in the most favourable stage for starting treatment, namely before clinical appearances are characteristic, or serum reactions have become positive. If, and when, practitioners and the lay public realize the great advantage of commencing treatment in the sero-negative stage, both in the smaller amount of treatment required and the greater certainty of achieving complete eradication of the infection, the day will not be very distant when syphilis has become as rare as chlorosis.

Serum diagnosis

In the past twenty years the views of syphilologists and pathologists on the relative values of the numerous serum tests for syphilis have undergone some important changes. The tests are divisible into two main classes, complement-fixation or Bordet-Wassermann (B.-W.), and flocculation. At the laboratory conference held in 1923 by the Health Organization of the League of Nations it was agreed that the best flocculation test was neither so sensitive nor so specific as the best B.-W. From then onwards, however, the flocculation tests were gradually improved, and, as a result of laboratory conferences under the same auspices in Copenhagen in 1928 and in Montevideo in 1930, it was agreed that, in the hands of their authors, the best flocculation tests were now superior to the best B.-W. in sensitiveness, and equal in specificity. In 1932, influenced by results obtained at these two conferences, the Health Organization's Reporting Committee on Syphilis presented a report in which they concluded that, in extraordinary circumstances where it is impracticable to test the serum by more than one method, a flocculation might replace the B.-W. As, however, some sera give a negative reaction by a flocculation test, but a positive by a B.-W.—though the reverse is much more common—it is advisable to employ both a flocculation and a B.-W. test.

Since then the position has changed again somewhat. Whereas no flocculation has been invented which is as specific as, but more sensitive than, those compared at these Conferences, and whereas none can seriously challenge the position of the Kahn, Hinton, Meinicke-Klärungs (M.K.R. II), and the Müller-Ballungs (M.B.R.) tests, improvements have been made in the B.-W.

test increasing its sensitiveness without impairing its specificity. In consequence it might well have happened that, at the Laboratory Conference to have taken place in Copenhagen, in September 1939, the difference between the best Wassermann test would have proved in respect of sensitiveness much closer to the best flocculation test.

Even without any improvement in the sensitiveness of the complement-fixation method, however, I would still prefer to rely for a diagnosis of syphilis on a positive Wassermann rather than on a positive flocculation reaction.

Comparisons of serum tests for syphilis, which were begun by the Health Organization of the League of Nations, have proved a most valuable means of assessing their value. By revealing unsuspected weaknesses in methods hitherto believed by those who practised them to be superior to other methods, they must have had a very salutary effect on some of the collaborating laboratories. They have shown that no new test should be accepted until it has been proved at least equal in sensitiveness and specificity to the best so far extant by comparison with a large number of unknown sera, as was done at the laboratory conferences mentioned above, and in the tests of methods more recently conducted under the auspices of the U.S.A. Public Health Department.

In the past there has been too great a tendency to accept authors' valuations of their tests, and it has required the acid test of a comparison of methods on unknown sera, with the dispassionate judgement of independent observers, to convince some authors that their methods required drastic revision.

In the interpretation of serum tests it seems surprising that there should still be a tendency in some quarters to accept a single positive blood-reaction in a pregnant woman or in a new-born infant as diagnostic, without confirmatory evidence. In pregnancy the blood serum rather tends to become positive, especially with some methods, and the reaction must be regarded only as an indication for further investigation. In the case of the new-born infant the blood reaction has often been proved to be only a reflex of the condition of the mother's blood, and in large numbers of cases the positive reaction has died out, the infant showing no sign of syphilis. This is mentioned here because I know of cases in which medical officers responsible for the welfare of pregnant women and new-born infants have been regarded by V.D. specialists as almost guilty of negligence for refusing to treat for syphilis in cases in which the evidence, apart from the blood reaction, did not support a diagnosis of syphilis.

Effect of treatment in preventing the spread of syphilis, and its late effects

Data are now accumulating by which can be judged the effect of modern treatment on the incidence of syphilis, and in the prevention of the late effects of the disease.

As regards incidence, a good example of the effect of applying to a very high percentage of the infected in a community a prolonged treatment on lines calculated to result in a minimum of relapses is seen in Sweden. In 1918 the present law under which every infected person must undergo all the treatment considered necessary by the medical advisers came into force, and conditions have favoured its observance. In the five years 1915-19 inclusive the rates of incidence of primary and secondary syphilis per 10,000 of the population were 4.3, 4.4, 4.7, 10.2, and 5.6 respectively; in the five years 1931-35 inclusive the rates were 1.9, 1.3, 0.87, 0.72, and 0.67 respectively, and other statistics show that syphilis has now become a rare disease in Sweden. Similar success can be shown in Denmark, where also the authorities have been successful in compelling infected persons to undergo prolonged treatment.

But much less treatment than the amount now usually prescribed seems to be sufficient to reduce the rate of incidence of fresh syphilis. As is well known, in England and Wales there is free treatment of the infected, but no com-

pulsion to take it, and very large numbers of those dealt with at the treatment centres cease attendance before completion, many in fact before they have received even one course of 7 to 10 injections of an arsphenamine compound with corresponding bismuth or mercury. It has been supposed that those who ceased treatment prematurely must have again become infectious, and it has been suggested that they nullify the value of the country's anti-venereal measures so far as syphilis is concerned. The evidence seems to be against this supposition. It is generally agreed that the free treatment centres set up throughout the country have dealt with the great majority of the new syphilitic infections, and changes in numbers of new cases dealt with in a year probably parallel very closely changes in the incidence of fresh disease. Although, unfortunately, prior to 1931 the returns from the centres did not, in the cases dealt with for the first time, distinguish between old infections and fresh ones, it is probably fair to say that the early infections dealt with in the centres prior to 1931 were not less than 40 per cent of the total new cases, this being approximately the proportion which they constituted in 1931; such an assumption seems to be fair, considering that the ratio of early to late cases dealt with in the centres has steadily fallen since 1931.

Assuming then that the early syphilitic infections dealt with in the centres for the first time in 1920 were 40 per cent of the total new cases, the number was 19,120, and the number dealt with in 1938 was only slightly over one quarter of this figure. This evidence of a great reduction in the incidence of syphilis is supported by figures showing substantial declines in mortality of infants certified as due to syphilis, in positive reactions found by routine tests of the blood of pregnant women, and in the falls in the numbers of cases of congenital syphilis in infants and young children dealt with at the centres.

As regards the mortality of infants certified as due to syphilis, the rate per 1,000 live births in 1912 was 1.34; in 1917 it had risen to 2.03; and from then it declined steadily to 0.23 in 1937. Results of routine tests of pregnant women have shown declines in positive reactions wherever they have been carried out over a number of years. Thus, in Battersea, 3.5 per cent were positive in 1924, but only 0.7 in 1936; in Cardiff the positive reactions averaged 3.1 per cent from 1925 to 1928, but 1.8 in 1935; in Glasgow 4.9 per cent were positive in 1925, but 1.8 in 1935. Fildes' tests of a sample of 386 adult women in the East End of London before 1913 resulted in 5.1 per cent being found positive, and in Cruickshank's tests of women at a maternity hospital in Glasgow in 1920-1, over 9 per cent were positive. Thus the evidence of a substantial fall in the incidence of syphilis in Great Britain is strong, and the figures suggest that a much smaller amount of treatment than one would prescribe to insure eradication of the disease in as nearly as possible 100 per cent of cases renders the majority of patients permanently non-contagious. That a relatively small amount of treatment often suffices apparently to eradicate the disease is supported by the number of cases in which patients, who have returned to clinics many years after receiving less than half a dozen injections of each type of drug, have been found completely free from signs and with negative serum reactions.

Altogether, our evidence is that the amount of treatment received in English centres by the average early case of syphilis, though much less than the amount prescribed, is gradually making syphilis in this country, as in Sweden and Denmark, a rare disease.

A question of importance is whether or not a relatively small amount of antisymphilitic treatment can be expected to protect the infected against disastrous late effects. The evidence seems to be that it can.

In published statistics relating to the treatment which was given in the early stages of their infection to patients suffering from cardiovascular and neuro-syphilis, one fact which always stands out prominently is the very low proportion of such cases in which it amounted to more than a few injections. As

an example may be cited the investigations on these lines which have been reported by Weatherby, Müller-Deham, Madden, and Smith and Kimbrough respectively. The total number of cases dealt with by these workers was 936, of which all but 127 had cardiovascular or neurosyphilis, and of 931 cases in which the early treatment appears to have been known fairly accurately, only 8 appear to have received more than 10 injections of an arsphenamine compound in the primary and secondary stages. Five other cases are stated to have had treatment with '606' in the early stages, but the amount is not stated.

Evidence from another direction appears to be afforded by the figures relating to mortality in England and Wales from general paralysis of the insane, tabes, and aneurysm. The very great increase in the incidence of syphilis in England and Wales during the war of 1914-18, when over 80,000 men of the British Expeditionary Forces were treated for early syphilis, would lead one to expect now a considerable increase in mortality from these three late effects. The figures (see Table below) show that, in males, from the year 1922 to 1938 the crude death-rate per million for general paralysis of the insane and tabes dorsalis fell fairly steadily, and that only that for aneurysm rose. In females, during the same years, the rate for general paralysis of the insane and tabes also fell, but not so rapidly, and in aneurysm it rose until, in 1937, it was nearly $2\frac{1}{2}$ times the rate in 1922.

Crude Death-rates, per Million Persons, from General Paralysis of the Insane, Tabes Dorsalis, and Aneurysm in Males and Females, for the Years 1922, 1927, 1932, and 1937

[Rates are to nearest whole numbers]

YEAR	GENERAL PARALYSIS		TABES		ANEURYSM	
	MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
1922	77	15	36	7	45	11
1927	65	14	34	7	47	13
1932	45	11	33	7	50	16
1937	30	12	24	5	51	25

On studying these figures the natural thought is that the declines in mortality from general paralysis of the insane and tabes respectively are to some extent attributable to pyrogenetic and general antisyphilitic treatment, especially by pentavalent arsenical compounds, begun when symptoms of neurosyphilis became manifest; also that, since little can be done by antisyphilitic treatment to prevent death from aneurysm after it has been diagnosed, the increased mortality from this cause is reflecting more closely the increased incidence of new infection in the years 1914-18. But, whereas the increase in the mortality of males is by no means so great as one would have expected from one's knowledge of the increased incidence during the war years if no preventive influence had been at work, that in females does seem to reflect the great increase in incidence which, one judges, must have occurred also in this sex. It seems reasonable to suppose that the difference between the two sexes in respect of changes in rates of mortality must be due to the fact that, at the time of first infection, most of the males were serving with the armed forces and were brought under treatment, but that only a low proportion of the females infected at that time were treated.

In the military Venereal Diseases Hospitals in the war of 1914-18 the treatment given to an early case of syphilis consisted of no more than one of the courses now prescribed in an average civilian Venereal Diseases Treatment Centre, and, although it is much less than would be prescribed in normal circumstances, it seems probable from the above facts that it has so far prevented the development of late effects in a high proportion of cases.

GONORRHOEA

Keratoderma blennorrhagica is relatively rare. It is a complication of gonorrhoea which seems always to be accompanied by some arthritis. The feet are chiefly affected, though the condition may become generalized. The skin becomes tough, and a number of nut-brown dome-shaped nodules appear in it, varying in size from a large pea to the diameter of a silver threepenny piece. The nails may become enormously thickened.

The condition, though it is not syphilitic, improves under arsphenamine treatment. During the war of 1914-18 it seemed to become rather more common, but in recent years has again become rare, and with the general use of sulphonamide treatment mentioned below it should practically disappear.

Until the development of the sulphonamide treatment gonorrhoea was a problem in which the outlook was by no means hopeful. In this country there was no evidence that any headway had been made in preventing its spread, and in this respect we seemed to have fared no worse than Denmark or Sweden in which compulsory treatment laws appear to have been administered very efficiently.

Success in treatment depended very largely on skill and careful attention to small details and, even with these, was too uncertain for the comfort of mind of either doctor or patient. With all care, also, gonorrhoea took a serious toll in blindness of infants; crippling through arthritis; chronic ill-health through pelvic inflammation, sterility through epididymitis, prostatitis, and salpingitis, and domestic unhappiness through the above causes, and outbreaks of vulvo-vaginitis of children. Now the outlook has changed; under a proper administration of sulphonamide preparations, especially 2-sulphanilylamino-pyridine, commonly known as M & B 693, the duration of the disease is shortened to a comparatively few days, and the incidence of complications reduced to a minimum.

In clinics it can reasonably be expected that such results will now be achieved in a high proportion of cases, and the prospects of making gonorrhoea a very minor problem would be rosy, if the majority of patients attended treatment centres. Unfortunately there is evidence that many practitioners are now treating gonorrhoea with sulphonamide remedies in a very haphazard way, often with doses too small to be permanently efficacious, and are not insisting on the very strict tests of cure which all who have studied the effects of these remedies in large numbers of cases believe to be essential. The result may be the creation for a time of large numbers of symptomless carriers who will continue to spread the disease.

SOFT CHANCER, GRANULOMA VENEREUM, AND
GANGRENOUS BALANITIS

Soft chancre is another bacterial disease which responds to sulphonamide treatment, and, thanks to this and to dmeclos treatment, the disease presents no difficult problem.

Granuloma venereum and gangrenous balanitis are of relatively small importance since neither is common. The former yields to intramuscular injections of antimony compounds such as foudadin and anthiomaline, and the latter to aeration with hydrogen peroxide solution.

LYMPHOGRANULOMA INGUINALE (L.I.) AND WAELSCH
URETHRITIS

There appears to be no evidence of any important increase in the incidence of L.i. in Great Britain where it has always been relatively uncommon. The evidence now accumulating that this relatively intractable condition yields to

sulphonamide treatment gives reason for hope that, in other countries, its importance will diminish considerably.

Waelsch urethritis, which appears from the description by Glingar to be identical with the condition commonly referred to in Great Britain as sago-grain or millet-seed urethritis, is of interest chiefly because of its possible relationship to trachoma and inclusion blennorrhoea on the one hand, and to L.i. on the other. The relationship to L.i. is suggested by the fact that, according to Frei, Wiese, and Klestadt; Bezecny; Ross; and others urethral discharge from cases of Waelsch urethritis, when made up according to the directions for the preparation of Frei antigen, and injected into the skin in cases of L.i., evokes an allergic skin reaction like that caused by antigen known to contain the virus of L.i. Cases have also been reported by Bezecny, Fahlbusch and Zierl, and Ross of an allergic skin reaction produced in cases of Waelsch urethritis by L.i. antigen. Inclusion bodies somewhat resembling those believed to be the cause of L.i. have been described in Waelsch urethritis, trachoma, and inclusion blennorrhoea, though it is not believed that they are identical. The appearance of the urethral mucous membrane in Waelsch urethritis, as in trachoma, is granular, and the disease is very intractable unless a sulphonamide compound is administered. The suggestion that Waelsch urethritis is L.i. of the urethra seems to be opposed by the fact that it does not lead to severe fibrotic changes such as occur at any rate in the rectum when this is infected with the virus of L.i.

SUMMARY

From the above survey it will be gathered that the outlook in venereal diseases is decidedly hopeful, and that we can look forward confidently to a future in which syphilis and gonorrhoea will play only minor roles either as killing or crippling diseases.

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UROGENITAL DISEASES, NON-VENEREAL

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MALE STERILITY

Testicular biopsy

Several advances have been made in this subject during 1938-39, both in diagnosis and treatment. One of the most important of these has been the use of testicular biopsy as a means of throwing light on the condition of the tubules. Testicular puncture has a very limited value in differentiating cases of aspermatogenesis from blockage, and provides the andrologist with no information concerning the state of the testicle. Testicular biopsy, on the other hand, can be carried out with little more difficulty than puncture, and gives much more valuable information. It can be performed under local anaesthesia.

After infiltrating the scrotum with a 2 per cent procaine hydrochloride (novocain) solution, an incision is made, and deepened until the glistening coat of the tunica albuginea is seen. This is then punctured with a trocar, or with a pointed tenotome. By a slight pressure on the testicle, a small button of tissue can be made to extrude; this is cut off by means of fine iridectomy scissors, and, after hardening in Bouin's solution, is submitted to microscopic examination. The operation is concluded by closing the skin incision with one or two sutures, and applying Whitehead's varnish. Haemorrhage does not usually constitute a difficulty, and the only pain felt is at the moment of puncture of the tunica albuginea.

GONADOTROPHIC HORMONE IN THE TREATMENT OF MALE SUB-FERTILITY

Progress has been made in the treatment of the sub-fertile male by the use of gonadotrophic hormone. The fact that this hormone is produced by the anterior lobe of the pituitary only would suggest that, when treatment is indicated, extracts of anterior lobe pituitary should always be used. Animal experiments have shown, however, that gonadotrophic substances capable of stimulating testicular function can more conveniently be obtained from non-pituitary sources. The available substances vary greatly, both in origin and activity. For practical purposes four sources of gonadotrophic substance must be distinguished: (1) The anterior lobe of animal pituitary glands (A.L.P.); (2) the urine of pregnant women (P.U.); (3) the urine of menopausal or bilaterally oophorectomized women (O.O.); and (4) mare's serum obtained during certain stages of pregnancy (M.S.).

All of these extracts have been used with success in cases of male sub-fertility. Experience shows that pituitary gonadotrophic hormone is of little therapeutic value if this hormone is being excreted in normal or excessive amounts in the urine. On the other hand, it is found that, in some men who excrete pituitary gonadotrophic hormone, spermatogenesis may be stimulated by means of P.U. A practical application of these findings is that the extract prescribed when gonadotrophic excretion is scanty or absent is either M.S.

or A.L.P., or a combination of both; whereas when the urine contains a normal or excessive amount of gonadotrophic hormone, the agent prescribed is P.U.

In cases in which the aim of treatment is to stimulate secretion of testicular hormone (for example, in partial infantilism), the presence or absence of gonadotrophic secretion in the urine does not influence the choice of extract; in such cases it is advisable to administer a mixture of P.U. and A.L.P.

Gonadotrophic extracts may reasonably be used in the following conditions: (1) undescended testis; (2) azoospermia not associated with blockage of the passages or retention of the testis in the abdomen, and (3) deficiency of spermatogenesis manifested by azoospermia, teratozoospermia (the presence of many abnormal or immature spermatozoa), anisozoospermia (excessive variations in the size of normal spermatozoa), or asthenozoospermia (spermatozoa of poor vitality).

DYSCYESIS

Many marriages are not sterile in the usual sense of the word, yet remain childless because of repeated abortion. The name dyscyesis is given to the tendency to early abortion which occurs in successive pregnancies without any detectable lesion or trauma. Dyscyesis may be due either to endocrine disturbances or to localized disease of the female genital tract. It may also be due to defective chorionic development, in its turn the result of some constitutional defect of the gametes.

When studying the clinical histories of a number of patients whose semen contained abnormal or defective spermatozoa, it has been found that in a surprisingly high proportion of cases the wives have suffered from repeated miscarriages. This suggests that sub-normal semen may be adequate for the attainment of conception, yet inadequate for the normal development of the ovum. Moench, and Williams and Savage have already recorded similar observations made on sub-fertile bulls. If therefore the wife of a husband who has previously been reported as sub-fertile becomes pregnant, the risk of miscarriage must also be borne in mind. By the institution of prompt treatment in the form of injections of chorionic hormone a miscarriage may frequently be averted.

STERILIZATION OF THE MALE

Although the technique of vasectomy for sterilization is extremely simple, experience has shown that it not infrequently fails to achieve its purpose. Regeneration of the continuity of the vas has occurred in two or three cases undertaken by the writer, even when an inch of vas had been resected. Other cases of apparent failure after sterilization have been due to the fact that a few spermatozoa have remained in the semen even after three ejaculations have occurred. In order to avoid the former of these two pitfalls, J. E. Strode of Honolulu has recommended that, after division of the vas, its lower end be fixed to the skin incision, so that the ends of the vas lie in different planes and there is no tendency for epithelialization to occur along the sheath of the vas. To avoid the second danger specimens of semen should be submitted to the laboratory for examination, and contraceptive measures only left off when these are found to be free from spermatozoa.

HORMONE TREATMENT OF PROSTATIC ENLARGEMENT

Repeated doses of oestrin produce certain changes in the prostate of mice and monkeys which recall those occurring spontaneously in man in the development of an enlarged prostate. It has also been shown that animals can be protected from the effects of oestrin by the simultaneous use of male hormone. This has led to the hope that the male hormone might exert an

influence on prostatic enlargement in human beings. So far, however, treatment along these lines has not produced any striking results.

A test carried out by the Medical Research Council has given negative results. When judged by such objective data as the residual urine and the size of the prostate, estimated by rectal examination and cystoscopy, no change was found, even after the administration of such large doses as 75 mg. twice weekly over a period of three months. Patients submitted to such treatment usually stated that they felt better in general health, and sometimes considered that their urinary symptoms had been ameliorated. Clinical examination, however, revealed the fact that the prostatic condition was either the same, or had even progressed, so that in some instances a prostatectomy had become necessary. Doubt must therefore be felt as to whether the human condition affords an exact parallel to the changes brought about in animals by the administration of oestrin. Further work will be required before this doubt is set at rest.

It is only fair to add, however, that other observers have reported more favourably of the results of hormone treatment than has the special committee of the Medical Research Council.

PYELITIS

The treatment of urinary infections in general by means of mandelic acid and the sulphonamide group of drugs still continues to give such good results that older methods, such as the use of a ketogenic diet, have fallen into abeyance. Fortunately, mandelic acid and sulphanilamide are not so much rival methods of treatment as complementary remedies to be used in different types of infection. Whereas mandelic acid has been proved ineffective in *Proteus* infections, these are often amenable to treatment with sulphanilamide. Similarly, infections with *Streptococcus faecalis*, which do not respond to sulphanilamide, are generally improved by the use of mandelic acid.

A great advantage of the sulphonamides is that they can be employed during the acute stages of an infection at a time when acidifying the urine might cause a temporary aggravation of symptoms. Sulphanilamide is effective in an alkaline urine.

Of the relative merits of the different varieties of these agents available it is not possible to speak with the same assurance, but it may be said that, on the whole, calcium mandelate is tolerated better by patients with poor digestions than are some of the older preparations.

In all cases it is of the utmost importance to carry out daily, or twice daily, estimations of the pH of the urine of patients on mandelic acid treatment, since the reaction of the urine is liable to change within a short space of time, and a slight increase in the pH reading may render the remedy ineffective. The most convenient bedside method of testing is by means of a methyl red indicator. If a few drops of this reagent added to an inch of urine in a test-tube produce a faint rose colour, the reaction is correct; an orange tint shows that the pH is too high, and an intense pink that it is unnecessarily low.

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PART II

DRUGS

SOME MODERN DRUGS

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HYPNOTICS, SEDATIVES, AND ANAESTHETICS

The production of new synthetic hypnotics, chiefly of the barbiturate group, has somewhat diminished recently. There is still, however, an embarrassing number of such remedies, and the difficulty of selection is increased because the same substance may be known under different proprietary names.

Where it is desired to assist the patient to go to sleep quickly and to avoid drowsiness on the following day it is essential that the drug should be rapidly absorbed and rapidly excreted or destroyed in the body. Of the newer remedies evipan in tablet form for oral administration is one of the most satisfactory. When a more prolonged sedative action is desired, phenobarbitone sodium, nembutal, and amytal are among the more popular, the two latter being commonly used in larger doses for the production of 'basal anaesthesia'. Care should be exercised with regard to the administration of large doses of these drugs, especially in the presence of severe sepsis, for they are all to a greater or lesser degree toxic to the liver and kidney, and fatal cases of liver destruction with jaundice have been reported after their use.

Avertin continues as the most popular and generally used substance administered *per rectum*, particularly in cases of thyrotoxicosis. Now that it is no longer employed for the production of full anaesthesia, unpleasant or toxic consequences are rare.

Of the substances used for induction of anaesthesia by intravenous injection evipan continues to hold its own. Deaths have been recorded following its use, especially where very large doses have been employed in order to produce prolonged anaesthesia, but within its own sphere, i.e. for full anaesthesia in short operations, or for induction followed by inhalation anaesthesia in prolonged operations, it is most satisfactory. A sulphur-containing compound, pentothal, has for some time been used as an alternative to evipan, and it is claimed that it is in some respects superior to the latter.

Ethylene has for some time been employed for inhalation anaesthesia as an alternative to nitrous oxide, though many patients object to its smell.

In recent years cyclopropane has come to be used more commonly. Its use necessitates a closed inhalation system, but it has the advantage that it can be given with high percentages of oxygen so that the element of asphyxia, formerly too common in inhalation anaesthesia, can be eliminated. Except in low concentration this gas has toxic effects on the heart muscle and needs skilled administration; the risk of explosion by sparks is as great as with ether and ethylene. Nevertheless the introduction of cyclopropane with consequent elimination of irritation of the respiratory passages is a distinct therapeutic advance.

ANALEPTICS, MEDULLARY AND VASCULAR STIMULANTS

Various substances have been used in the attempt to restore failing respiration and circulation, especially in severe infections, after anaesthetics, and in cases

of overdosage of hypnotics. Formerly only strychnine, caffeine, and solutions of camphor and ether in oil were used to any extent, but they were not very satisfactory.

Pyridine- β -carboxylic acid diethylamide (coramine, anacardone) and pentamethylenetetrazol (cardiazol, metrazol) have almost entirely supplanted these, and are now very extensively employed both by mouth and by injection. It is unfortunate that the names given to these substances suggest that their chief action is on the heart; this is not the case. Very similar in its effect on the brain and medulla is the natural substance picrotoxin. All these drugs are essentially stimulants of the central nervous system, tending to restore consciousness and to augment respiration and blood pressure by their action on the medulla. How far this action on blood pressure via the medulla is sufficient to be of clinical importance is at present difficult to assess. Animal experiments suggest that it is not great, for the dosage required to produce appreciable effects is much greater proportionally to body weight than is employed in human therapeutics. As stimulants to accelerate recovery from anaesthetics and to augment breathing there would appear to be little to choose between picrotoxin, cardiazol, strychnine, and coramine. As antidotes to barbiturates such as nembital, animal experiments indicate that picrotoxin and cardiazol are far superior to the other analeptics; indeed there is some evidence that coramine and benzedrine may be actually harmful.

In addition to these drugs the action of which is mainly or entirely central there are several the action of which on the circulation is mainly peripheral, that is on the heart and blood vessels. Their action simulates, to a greater or lesser extent, that of adrenaline. Of these drugs the best known is ephedrine the use of which in restoring the circulation, by combating the fall of blood pressure which may occur in spinal anaesthesia, is well established. Allied in action are sympatol and veritol the clinical applications of which are not yet sufficiently defined; they may, however, prove to have a definite place in therapeutics for restoring blood pressure not only after haemorrhage or shock but also in collapse following acute infections.

In many cases of shock and collapse, e.g. after operations, and in toxic conditions, e.g. after burns, preparations of adrenal cortex such as eucortone, cortin, and desoxycorticosterone acetate, have proved of value. Much remains to be done in assessing the value of remedies for this purpose, the high cost of these preparations being a difficulty in the way of this.

DRUGS ACTING ON PLAIN MUSCLE

Perhaps the drug most widely used for its action in causing contraction of plain muscle is pituitary posterior lobe extract. Now that its two important constituents—the oxytocic, or uterus-contracting principle, and the pressor, or arteriole-contracting principle—can be separated it has been found that the substance causing contraction of the muscle of the gut is either identical, or constantly associated with the latter constituent. The antidiuretic principle is similarly associated. It is thus possible to cause powerful contraction of the uterus without producing any considerable rise of blood pressure.

The vasopressor substance which causes contraction of the plain muscle of the intestine is now much used alone for combating distension of the abdomen by improving gut tonus and aiding peristalsis. The action is directly on the muscle. Intestinal tonus and peristalsis may be augmented also by drugs which affect the vagal neuromuscular mechanism. Acetylcholine is probably the substance which in the body transmits the nervous impulse from the vagus to the intestinal musculature. When injected it causes increased peristalsis, but in practice it is less used than the allied substance doryl. Physostigmine has long been used to stimulate peristalsis; it acts by preventing the destruc-

tion in tissues of the naturally formed acetylcholine, and hence conserving and augmenting its action. More recently the artificial alkaloid prostigmin has been employed for this purpose and, owing to its less effect on the heart and bronchi, it is generally preferable to physostigmine.

The maximal effect is produced when pituitary extract or pitressin is administered in conjunction with prostigmin. An excellent example of synergism is provided; if half the usual doses of prostigmin and of pitressin or pituitary extract are injected simultaneously, the resulting effect is usually much greater and more satisfactory than that of a normal dose of either drug alone.

In addition to their action on intestinal peristalsis doryl and prostigmin have proved their value in post-operative distension of the bladder. Active contractions are produced which usually result in overcoming the inability to micturate.

The problem of relaxing spasm of plain muscle frequently arises. When, as in certain forms of colic, e.g. biliary, renal, and intestinal colic, there is severe pain full doses of morphine are commonly administered. This practice is not based on sound therapeutic principles. Though relief of pain is urgently required, it should be borne in mind that morphine, while it relieves pain by central cerebral action, causes at the same time an increase in tone of plain muscle and thus prevents the passage of the irritant, e.g. a stone. Furthermore, it has been shown that morphine, by causing contraction of the sphincter of Oddi, causes a rise of biliary pressure, and thus may have undesirable effects on the liver.

It is far better practice in most cases to endeavour to cause relaxation of the tonus of the plain muscle. Not only is the pain thus diminished or abolished, but the irritant substance is no longer gripped, and can be passed on by peristalsis or by the pressure of secretions behind it.

Rapid, though transitory, relaxation with considerable relief of pain may be produced by inhalation of amyl nitrite. More satisfactory, because longer, effects can be obtained by administering glyceryl trinitrate (nitroglycerin). In order that the drug may be rapidly absorbed it is important that the tablet should be sucked or chewed, not swallowed at once. The drug is absorbed fairly rapidly from the mouth, and much more quickly than when it is swallowed.

For more prolonged effects papaverine, one of the opium alkaloids, may be used. In contrast to morphine it causes relaxation of plain muscle. A synthetic compound, eupaverin, with a similar action is stated to be less toxic.

Plain muscle of the intestinal, biliary, and renal tracts can also be relaxed by drugs such as atropine which paralyse or diminish the activity of the vagal nerve mechanism which is motor to the organs, or by drugs allied in action to adrenaline which simulate the inhibitory effect of the sympathetic nerve supply. Atropine and hyoscine are commonly employed, but the former especially is not very popular in full doses, probably on account of its central or cerebral stimulant action. Atropine methylnitrate (eumydrin) has already established itself as a very valuable remedy in the treatment of congenital pyloric stenosis and its use largely replaces operation.

For colicky and spastic conditions there are numerous proprietary remedies consisting of mixtures of papaverine or one of its allies or derivatives, with an ally or derivative of atropine and small doses of morphine, omnopon, or a barbiturate. Many of these mixtures have proved to be very satisfactory in the relief of biliary and renal colic.

By mimicking the action of the sympathetic nervous system and relaxing plain muscle ephedrine is also of value in the relief of biliary and renal colic (compare its action on the bronchial muscle in asthma). It has also been used with excellent effects in combination with atropine and papaverine.

DRUGS ACTING ON MUSCULAR WEAKNESS

In Addison's disease

Several crystalline substances have been isolated from crude extracts of the adrenal cortex, the most active being corticosterone. Desoxycorticosterone—a related substance—has been synthesized, and has been shown to be active in the treatment of patients with Addison's disease (Levy Simpson). Clinically it is found that 5 mg. of desoxycorticosterone acetate is equivalent in effect to 10 c.cm. of cortical extract (cortin). Treatment is more effective if the patient receives in addition a low potassium diet and extra sodium chloride.

Desoxycorticosterone acetate is given (*a*) by intramuscular injection (5 mg. dissolved in 1 c.cm. of sesame oil); (*b*) by implantation of four 50 mg. tablets in the subcutaneous tissue of the abdomen, when an effect lasting two months is obtained; and (*c*) by injection of a solution of the drug in benzyl alcohol.

In myasthenia gravis

The prostigmin treatment continues to be the most satisfactory. Its efficacy is increased by combination with ephedrine. When large doses of prostigmin are required, or in susceptible subjects, colicky pain is sometimes produced. Atropine administered with the prostigmin injections diminishes attacks of colic.

Oral administration of prostigmin is effective, but by this route a very much larger dosage is required—usually some thirty times greater than that needed by injection.

In Thomsen's disease

Some patients are much benefited by the administration of quinine hydrochloride. The tendency of the muscles to 'lock' is greatly diminished. The mode of action of the drug in this condition is unknown.

In familial periodic paralysis

It has been found that the attacks of paralysis in this disease are associated with a fall in the serum potassium, and the administration of potassium salts brings about rapid recovery in the power of the muscles. The low serum potassium is not in itself the cause of the paralysis, as low values have been produced in normal people without any paralysis appearing. The site of action of the potassium is not known, but the evidence suggests that it has a central effect on the nervous system, rather than a peripheral one on the muscles or neuromuscular junctions (Pudenz *et al.*).

Potassium chloride—five to ten grams—dissolved in water, given by mouth, will bring about recovery in a half to two hours. If given intravenously, the effect is much more rapid, but the patients complain of severe pain along the course of the vein.

Attacks can also be terminated by the injection of acetyl- β -methylcholine chloride (mecamylol) or carbaminoylcholine chloride (doryl), without the administration of potassium. The serum potassium rises as power returns in the muscles.

In certain cases there is a relation between carbohydrate intake and attacks of paralysis. Taking much sugar at night may cause an attack but, if potassium is given simultaneously, this can be prevented. Sleep is also a factor; thus, if the patient keeps awake, the attack does not occur.

ANTACIDS

Many patients have suffered from excessive administration of alkalis. Four grams (60 grains) of a common alkaline powder will neutralize $\frac{3}{4}$ litre (one pint) of gastric juice, and many patients take much more than this quantity several times daily. In general, a dose of 2 g. (30 grains) should not be exceeded, especially in middle-aged or elderly subjects whose capacity for elimination by the kidney is likely to be low. When alkali in excess is administered, moderate to considerable degrees of uraemia are common. When there is duodenal or pyloric spasm due to the irritation of an ulcer, belladonna, both because it relaxes spasm and inhibits acid secretion, is of considerable value.

There has been much search for some preparation which, while inactivating or temporarily neutralizing the acid of the gastric secretion, will not result in producing alkalosis. The chief available preparations are aluminium hydroxide and magnesium trisilicate. Much depends on the degree of dispersion of the colloidal particles; with good preparations the clinical results are very satisfactory.

Aluminium hydroxide

This is obtainable as a colloidal powder, which is insoluble in water, neutral, and amphoteric, and completely non-toxic. Experiments *in vivo* have shown that it combines with 12 times its volume of N/10 HCl within half-an-hour.

The early satisfactory reports from the use of aluminium hydroxide have been confirmed by recent clinical reports which have shown that it produces striking symptomatic relief from pain, nausea, and vomiting, even in long-standing cases of peptic ulcer, and that the relief obtained is almost immediate.

The action of aluminium hydroxide in gastric disorders associated with hyperacidity is somewhat complex, and may be briefly summarized as protective and demulcent to the gastric mucosa; antacid; and adsorptive to toxins. The colloidal form of the drug possesses considerable buffering power. The physico-chemical properties of the colloidal gel formed when aluminium hydroxide mixes with the stomach contents effect adsorption of the hydrochloric acid, with a consequent immediate rapid decrease in the functional acidity of the gastric juice, and a more gradual subsequent reduction. The pH cannot go beyond neutrality, and the increase is to approximately pH 4. The processes of digestion are therefore not greatly affected. As a result of interaction between the drug and the gastric hydrochloric acid, some aluminium chloride is formed which, in the alkaline intestine, is again broken up into aluminium hydroxide and chloride; the latter is reabsorbed. The contention that gastric hydrochloric acid is carried through the intestine and excreted has not been proved.

Production of alkalosis, systemic poisoning from the aluminium moiety, disturbance of the acid-base metabolism, or the formation of intestinal concretions are stated not to occur, even from the use of massive doses of, or prolonged treatment with, aluminium hydroxide.

Besides its antacid properties, the drug in its gelatinous state in the stomach forms a protective coating to the mucosa. Its astringent effect is said to assist in arresting haemorrhage, and in the healing of ulceration.

With regard to clinical results, apart from the symptomatic relief obtained, there is radiological evidence of the rapid disappearance of peptic ulceration with efficient treatment, and it is claimed that relapses appear to be relatively less common than after the use of ordinary alkaline mixtures.

Magnesium trisilicate

This synthetic product possesses an action similar to that of aluminium hydroxide, with much greater adsorptive properties than those of natural silicates. In the stomach it reacts with hydrochloric acid to form silicon dioxide; the latter, on entering the duodenum, has a marked adsorptive effect on toxins

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THE PHARMACOLOGY OF SULPHONAMIDE DRUGS

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SULPHONAMIDE COMPOUNDS

The introduction and development of drugs of the sulphonamide group undoubtedly constituted the most remarkable advance in recent therapeutics. Many attempts had previously been made to effect sterilization of the blood stream, but to Domagk and his co-workers belongs the credit for having first rendered this possible. Employing a water-insoluble basic azo-dye, sulphamido-chrysoidine (to which the term prontosil and later prontosil rubrum was applied), Domagk found that mice infected with lethal doses of haemolytic streptococci survived when given intraperitoneal injections of this dye.

Prontosil, first introduced into therapeutics in 1935, is suitable for oral use. For parenteral administration a water-soluble preparation, prontosil soluble, was later introduced. Although prontosil proved so active against haemolytic streptococci in the living organism, it appeared to have little or no bactericidal effect *in vitro*. The explanation of this was suggested by Tréfouël *et al.* (1935) who put forward the hypothesis that the activity of the drug was due to that part of the molecule liberated in the body and which consisted of a sulphon-amido group attached to one benzene nucleus, *p*-aminobenzenesulphonamide, or, as it is now generally called, sulphanilamide. These workers tested the therapeutic efficacy of sulphanilamide and found it to equal that of prontosil. This finding was confirmed by many other workers. The surprising discovery was thus made that the colourless relatively simple moiety, sulphanilamide, and not the dye was the active principle of prontosil.

It must be stated, however, that Domagk maintains that prontosil rubrum has characteristic and superior properties associated with the azo-dye linkage, and not attributable solely to its liberation of sulphanilamide in the organism. This contention, refuted by many authorities, is somewhat supported by the fact that compounds of the sulphone type, such as 4:4' diaminodiphenylsulphone, which are unrelated chemically to the sulphonamides, have similar bactericidal properties, and by the fact that, weight for weight, prontosil rubrum is more active than sulphanilamide.

The pharmacological actions and therapeutics of sulphanilamide have been the subject of intense investigations, and these have been taken as the standard against which other sulphonamide derivatives have been compared. Similar vast activity has taken place in the evolution of other sulphonamide derivatives, and many hundreds of these have been examined with a view to obtaining increased therapeutic efficiency, a wider field of application, and a lowered toxicity. Sulphanilamide consists of a benzene ring to the opposite ends of which are attached respectively an amino group and a sulphonamide group. The amino group is in the *para* position, and the activity of the compound is lost if the amino group is transferred to the *ortho* or *meta* positions. Among the sulphonamide compounds which have proved sufficiently effective for clinical trial are several which may be placed in three groups, as follows:

1. Those in which substitution has been made in the amino group. The chief members of this group are the original *prontosil rubrum*, *prontosil soluble*, *rubiazol*, *proseptasine*, and *soluseptasine*.
2. Those in which substitution has been made in the sulphonamido group. Of these the most important are *uleron*, *M & B 693*, and *albicid*. Unlike compounds in group 1, these do not appear to be broken down in the body into sulphanilamide and probably are in themselves active.
3. A further group must be mentioned which contains sulphone compounds. Though these are unrelated chemically to the sulphonamides, they have a similar therapeutic action. Examples are 4:4' diaminodiphenylsulphone and 4:4' diacetyldiaminodiphenylsulphone (*rodilone*).

Group 1

Sulphanilamide (*p*-aminobenzenesulphonamide or *p*-aminophenylsulphonamide) may for descriptive purposes be considered under Group 1. It has so far been the most widely employed of the sulphonamide compounds, and is known under a great variety of proprietary names including *prontosil album*, *prontylin*, *proseptine*, *streptocide*, and *sulphonamide-P*. Sulphanilamide is soluble in 1 in 125 parts of water and 1 in 37 of alcohol.

A great volume of clinical reports has been published on the use of sulphanilamide in different infections. Many of these are dealt with in their appropriate places throughout this work.

Prontosil rubrum (sulphamido-chrysoidine) and *prontosil soluble* (the disodium salt of 4'-sulphonamidophenyl-2-azo-1-hydroxy-7-acetylaminonaphthalene 3:6-disulphonic acid) belong to the original azo-dye complex chemical compounds, which, on dissociation in the body, liberate sulphanilamide. The claim of Domagk that these azo-dyes are therapeutically more effective than sulphanilamide has been noted above, and some other authors, as for example *Colebrook* and *Purdie*, consider them to be superior to sulphanilamide in the treatment of streptococcal infections. The consensus of opinion, however, would appear to be that sulphanilamide can produce all the therapeutic effects of *prontosil rubrum* or *prontosil soluble*, or is even more effective. The oral preparation, sulphamido-chrysoidine, is now rarely employed, but the soluble product may be useful in cases in which a rapid effect is required, in which the use of a preparation by mouth is precluded, as in severe vomiting, or in which absorption of the drug from the alimentary tract is insufficient. In cerebrospinal infections it has been found that the red *prontosils* do not pass from the blood to the theca as rapidly as sulphanilamide.

Rubiazol (6-carboxysulphonamido-chrysoidine) is a dye similar to *prontosil rubrum*, with an added carboxyl group. It appears to be broken down in the organism rather more slowly than *prontosil*, and therefore its action is milder. It is said to be relatively non-toxic.

Proseptasine (*p*-benzyl-aminobenzenesulphonamide), which is much less soluble than sulphanilamide, is also much less toxic both in animals and in the human subject. This relatively low toxicity is probably partly due to the fact that it is badly absorbed. Its activity against the haemolytic streptococcus is about the same as that of sulphanilamide, but it appears to be inactive against the meningococcus. Because of its low toxicity, *proseptasine* has been widely employed in clinical practice, but in the severer types of haemolytic streptococcal infection, and when the case is urgent, the use of sulphanilamide is preferable. It appears that its action in the body is not due to its reduction to sulphanilamide.

Soluseptasine [disodium-*p*-(γ -phenyl-propyl-amino)-benzenesulphonamide- α - γ -disulphonate], a colourless soluble compound for parenteral administration, is similar in effect to *proseptasine*. Good results have been reported from its use in streptococcal and meningococcal infections. As in the case of *prontosil soluble*, its use is only called for when oral administration is precluded. Large

amounts of both products must be injected, for example 60 c.cm. is equivalent to 3 g. of sulphanilamide. Since they are rapidly excreted, injections must be given at short intervals to maintain an adequate concentration in the blood.

Group 2

Uleron [4-(4'-aminobenzenesulphonamido)-benzenesulphondimethylamide], which was claimed by Domagk to be active against staphylococcal infections in rabbits and mice and in *Cl. welchii* infections, is at present chiefly employed in Germany in the treatment of gonorrhoea. A number of clinical reports have indicated that it is inferior to sulphanilamide, and it appears to be more toxic, in spite of the claims of some authors that it is less so. A serious disadvantage is that, unless it is employed in short courses, a generalized peripheral neuritis is liable to occur.

M & B 693, 2-(*p*-aminobenzenesulphonamido) pyridine, 2-sulphanilylamido-pyridine, or sulphapyridine, a more recent sulphonamide compound, appears to possess some definite advantages over the others. Most important of these is the fact that, while it is equally effective as sulphanilamide, or more so, against haemolytic streptococci and meningococci, it is highly active against several types of pneumococcus, whereas sulphanilamide is effective against only the Type III pneumococcus. Evans and Gaisford and other authors have reported excellent results in both lobar and broncho-pneumonia. Reid and Dyke, Robertson, and others have obtained successful results in pneumococcal meningitis. Whitby has shown that M & B 693 is more effective than sulphanilamide in staphylococcal infections in mice, and Bliss and Long and others have published reports of its successful clinical use in staphylococcal infections.

With regard to its effect on meningococcal infections Bryant and Fairman and Somers showed that it has an action in meningococcal meningitis, but its effect relative to that of sulphanilamide is not yet clearly established.

It is certainly more effective than sulphanilamide in gonococcal disorders, and it appears to be more active in *Cl. welchii* infections. Whitby has reported clinical improvement and prolongation of life in cases of subacute bacterial endocarditis.

With regard to toxicity, it appears that in lower animals M & B 693 is extremely non-toxic, and that it does not adversely affect the blood as sulphanilamide may do. Clinically, toxic effects so far reported have been remarkably few and relatively mild. Vomiting may occasionally occur as a result of gastric irritation, and, as the drug is very insoluble and so cannot be given parenterally, this may prove a disadvantage.

Although M & B 693 is more insoluble than sulphanilamide it is more rapidly absorbed and more slowly excreted.

It may thus be stated that M & B 693 is effective in the conditions in which sulphanilamide has proved its value, and has in addition an action in some conditions in which the latter is ineffective. It is the most active sulphonamide drug yet available for pneumococcal, gonococcal, and staphylococcal infections, and, according to Whitby, it has a greater chance of success than sulphanilamide when used empirically in infections in which a definite bacteriological diagnosis has not been made.

Albucid (*p*-aminobenzenesulphonacetamide) is said to be extremely free from toxic effects. Its chief use is in the treatment of gonorrhoea, and it appears to be of little value against the streptococcus.

Group 3

Members of this group of drugs which includes 4:4'-diaminodiphenylsulphone and its derivatives, though not related chemically to sulphanilamide, possess high bactericidal activity, but, because of their relatively high toxicity, they are not yet of great clinical importance.

MODE OF ACTION

Many hypotheses have been advanced to explain the mode of action of the sulphonamides, and these may be broadly grouped into those suggesting that the drugs act on the host and thus indirectly on the infecting organisms, and those suggesting that they act directly on the organisms themselves.

Action on the host

A considerable amount of work has been done in determining whether or not the sulphonamides stimulate the natural defence mechanism of the body. It is known that sulphanilamide itself does not produce in the body an anti-bacterial condition of any great duration, for the progress of infections induced by the inoculation of organisms a few hours after the discontinuance of repeated doses of the drug is less influenced than it is when a similar dosage is given at, and after, inoculation. It thus appears that, for its therapeutic effect, the drug must come into contact with the organisms in the body of the host.

Effect on leucocytes

The suggestion that the sulphonamide drugs may act by stimulating leucocytosis has been disproved. Britton and Howkins showed that sulphanilamide produced, if anything, a slight leucopenia. McIntosh and Whitby, employing M & B 693, showed that its intensive administration in mice produced no changes in the leucocyte count, and that the blood-picture was an inert one which implied neither stimulation nor depression of the bone-marrow. Since M & B 693 has been shown to have an effect *in vitro* in serum and broth as well as in whole blood, it would appear that leucocytes are not a primary necessity for its action.

Effect on reticulo-endothelial system

It has been claimed that stimulation of the activity of the reticulo-endothelial system of the spleen occurs in rabbits to which sulphanilamide is given, but McIntosh and Whitby, after numerous experiments in which the spleens of animals inoculated with living cocci and protected with M & B 693 were examined, could find no evidence to support this. Gross *et al.* found that splenectomy did not prevent the protective effect of sulphonamide compounds in mice infected with streptococci, and McIntosh and Whitby made similar observations with M & B 693 in mice infected with pneumococci.

Specific antibodies

McIntosh and Whitby showed that the quality, quantity, and speed of production of the immunity produced in animals cured by M & B 693 of a living infection seems to be fundamentally the same as that produced by orthodox active immunization. Moreover, the degree of immunity produced is unrelated to the dose of the drug, and is proportional to the number of organisms inoculated as it is in orthodox active immunization, being greater when large numbers of living cocci are inoculated and smaller when small numbers are given. The conclusion from this would appear to be that the sulphonamides have no stimulating effect on the defence mechanism of the body, and that they do not affect the production of recognized specific antibodies.

Anti-endotoxic action

The hypothesis that the sulphonamides exert an effect in neutralizing endotoxins elaborated by bacteria has received support from some quarters (Levaditi and Vaisman).

Effect on bacteria*Bacteriostatic or bactericidal action*

The antibacterial action of sulphonamide drugs is believed by many to explain their therapeutic effect. There are, however, many factors which prevent this explanation from being completely satisfactory.

Ample evidence has been adduced to show that sulphanilamide exerts a bacteriostatic effect on certain organisms *in vitro*, and, in higher concentrations, a bactericidal effect.

Levaditi and Vaisman pointed out that there are much more powerful antiseptic substances, for example proflavine, which have little toxicity for the mammalian body and have a similar rate of excretion to that of sulphanilamide, yet fail to cure a general infection.

The bacteriostatic and bactericidal effects of sulphanilamide vary according to the medium in which the tests are made. There is also a lack of parallelism between *in vitro* and *in vivo* actions of the sulphonamides, since prontosil rubrum is active *in vivo* but not *in vitro*, whereas sulphanilamide is active against the pneumococcus *in vitro* but not *in vivo* (Britton)

McIntosh and Whitby showed by a large number of *in vivo* and *in vitro* tests with M & B 693 and pneumococci that the drug is not instantly bactericidal nor even bacteriostatic, but that the restraining action of the drug on the organisms does not become evident for periods up to six hours.

Levaditi and Vaisman (1935) observed that sulphanilamide may cause capsular degeneration in streptococci. McIntosh and Whitby, while confirming this, could not confirm the claims of Telling and Oliver that these apparent capsular changes were accompanied by loss of type specificity and virulence.

There is apparently a quantitative relation between the effective dose of the sulphonamides and the number of bacteria affected: McIntosh and Whitby found that *in vitro* a concentration of 4.2 mg. per 100 c.cm. extinguishes an inoculum of 500 organisms, whereas a concentration of 16 mg. per 100 c.cm. eliminates 50,000.

With regard to a possible fixation of sulphonamides by bacteria *in vitro*, McIntosh and Whitby found no appreciable loss of M & B 693, even when considerable concentrates of organisms were added.

Neutralizing effect on metabolic factor

From the above facts it would appear that the sulphonamides do not act as simple germicides. McIntosh and Whitby have put forward the explanation that the time lag before the drugs become effective suggests that they slowly combine with, or neutralize, some food substance or enzyme essential to the survival of the organisms. The growth of the bacteria during the first six hours before the drug becomes effective would thus depend on the presence in the inoculated bacteria of a sufficiency of this essential factor to maintain their life during this period, since even very small numbers of bacteria exhibit this lag in high concentrations of the drug. Because, in an abundant medium such as the blood stream, an actual food factor would probably not be destroyed or fixed, McIntosh and Whitby suggest that the drug may inactivate the bacterial enzyme, of which this food factor is the substrate.

ESTIMATION IN BODY FLUIDS

A simple method of estimating the amount of sulphanilamide in the blood, urine, and other body fluids was evolved by Marshall *et al.* (1937a and b). This was based on diazotization of the sulphanilamide with nitrous acid and coupling the resulting diazo compound in acid solution with α -dimethylnaphthylamine, so as to produce a purplish-red azo-dye which can readily be estimated by

colorimetric comparison. This reaction depends on the presence of an amine group substituted in the benzene ring. The colour reaction can be detected in a solution containing one part of sulphanilamide in twenty million parts of water. A modification of this method involving the use of chromotropic acid was suggested by Scudi.

Disadvantages of such methods are that the diazotization reaction is tedious on account of the careful control necessary to avoid secondary reactions which interfere with development of the proper colour, and because neither α -dimethylnaphthylamine nor chromotropic acid is sufficiently stable or readily obtainable in a sufficient degree of purity to serve as a reliable reagent for routine work. Accordingly Werner suggested a new method which he claimed to be as accurate and sensitive as the diazotization methods, less tedious in performance, and involving the use of reliable clinical reagents.

Werner's method is based on the original observation made during the routine examination of the urine of a patient undergoing treatment with sulphanilamide that when Ehrlich's reagent, *p*-dimethylaminobenzaldehyde, is added, a copious orange precipitate is produced. It was found that the colour was proportional in intensity to the concentration of sulphanilamide and sensitive to about 1 part in 500,000. The colour is compared with that produced by treating standard solutions of sulphanilamide in distilled water with Ehrlich's reagent. The method can be applied, not only for the detection of sulphanilamide and its acetyl derivative in blood and urine, but also for M & B 693 and uleron.

ABSORPTION

The investigations of Marshall *et al.* (1937 a) have shown that, when taken by mouth, sulphanilamide is absorbed very rapidly from the small intestine, and that absorption is complete in about 4 hours. The concentration of the drug in the blood reaches its peak in about 3 hours, thereafter falling gradually to zero during the following 24 hours. It is generally held that, in daily divided doses, the drug reaches its maximal concentration in about 2 days. The parenteral administration of sulphanilamide has no advantages over its oral use.

Lucas and Mitchell state that the larger the individual dose, the higher is the peak of the blood concentration curve, and the earlier this peak occurs, and that maximal blood concentrations following single doses are not proportional to the dose, but increase only slightly on doubling or trebling the dose, provided that renal function is normal. They find that the maximal blood concentration is generally reached about 4 to 6 hours after a single 15-grain dose, and about 2 to 5 hours after a single 30-grain dose. In children the maximal concentration occurs 1 to 3 hours after a 10-grain dose. Provided that renal function is normal, repeated large doses (20 to 30 grains every few hours) do not raise the blood concentration above about 5 to 6 mg. per 100 c.cm. until the tissue fluids are saturated, which takes about 5 days. Impaired renal function causes the blood concentration to rise more rapidly and to higher levels, a fact which indicates the advisability of biological control of patients on sulphanilamide therapy.

To obtain optimal therapeutic results it is necessary to maintain a suitable concentration of the drug in the blood. Long and Bliss (1937 a and b) state that the optimal concentration in severe haemolytic streptococcal infections is 10 mg. per 100 c.cm., and, to obtain this concentration, a daily intake of 1 g. per 20 lb. body weight is necessary in adults. Banks states that for children this dosage must be increased to 150 per cent, and for infants to 300 per cent.

On entering the blood sulphanilamide quickly finds its way into all the fluids and tissues of the body. In the cerebrospinal fluid the concentration is about 75 per cent of that in the blood. The drug appears to pass as readily

into the cerebrospinal fluid of patients with bacterial meningitis as that of healthy subjects. The heart and skeletal muscle, liver, lungs, and spleen contain about the same concentration as the blood; the skin contains slightly less; the brain contains about 70 per cent; whereas fat and bone contain much less. The concentration in the blood cells is about 50 per cent greater than that in the plasma. Of the drug in the blood about 20 per cent is in the acetylated inactive form.

With regard to M & B 693, in animals this is absorbed more slowly than sulphanilamide (Marshall, *et al.*, 1938). The scale of dosage is similar to that of sulphanilamide. Since pneumococci may become resistant to the drug after prolonged treatment, it would appear to be preferable to secure an initial high concentration of the drug in the blood.

EXCRETION

The excretion of sulphanilamide is chiefly by the kidneys; it appears in the urine partly as the free base and partly in the inactive acetyl form. The investigations of Marshall *et al.* (1937 b) showed that the drug is excreted entirely by glomerular filtration, and that about 80 per cent of it is reabsorbed by the tubules. As a result of this the rate of excretion is partly dependent on the amount of diuresis, and not on the concentration in the blood; it is also dependent on the amount administered. It is possible to obtain and maintain much higher concentrations of the drug in the urine than in the blood. To obtain a good bactericidal effect in the urine concentrations of free sulphanilamide of from 30 to 40 mg. per 100 c.cm. of urine are necessary, but occasionally at lower concentrations there is a bacteriostatic action. After 2 to 3 days equilibrium is generally established between the amount of sulphanilamide ingested and the amount excreted. The excretion of sulphanilamide is complete in from 2 to 3 days, but is delayed when there is reduced renal function; as a result continued administration results in an accumulation of sulphanilamide in the blood, and toxic reactions appear. Since sulphanilamide tends to lower the carbon-dioxide combining power of the blood, i.e. to produce acidosis, and since it is more effective experimentally in an alkaline medium with a pH of 7 to 7.5 than in an acid medium, the simultaneous administration of sodium bicarbonate is advisable, particularly in elderly people with renal damage. M & B 693 is excreted more slowly than sulphanilamide, and reaches the cerebrospinal fluid more slowly.

Stewart, Rowke, and Allen, on the basis that at room temperature precipitation of excreted sulphanilamide in the urine has been demonstrated, suggested the possibility of formation of urinary calculi, if the volume of urine is allowed to become too small during treatment with the drug.

Stewart and Pratt state that free sulphanilamide is excreted in human breast milk in concentrations closely corresponding to the values present in the blood. When the drug was present in the milk in a concentration of 7 mg. per 100 c.cm., breast fed full-term infants showed no toxic manifestations. Indeed an infant cannot obtain an adequate therapeutic dose of the drug from the milk of a mother receiving an average dosage of sulphanilamide. Foster showed that, in one of his cases, when the blood concentrations of the drug were 4.3 and 5.5 mg. per 100 c.cm., the milk concentrations were 2.4 and 2.8 mg. per c.cm. respectively.

Bellows and Chinn investigated the concentration and distribution of the drug in the eye of dogs after oral doses of 0.2 g. per kg. of body weight. They found that the drug was present in all the ocular tissues and fluids within 15 minutes, and reached its maximal concentration in 6 hours. The drug is also excreted in the tears.

Investigating the transmissibility of the drug through the human placenta, Speert found that it passes readily to the foetus, the concentration of both the

free and acetyl forms in the foetal and maternal bloods reaching equilibrium within about 5 hours. The drug also passed rapidly into the amniotic fluid.

TOXIC EFFECTS

In drugs with such wide clinical applicability as those of the sulphonamide group, it is highly important that the prescriber should understand and recognize the toxic effects which they may produce. In the case of the sulphonamides these effects are many and varied and, in some instances, of a serious nature. They may for convenience be divided into mild and serious types.

The mild reactions include headache, vertigo, anorexia, nausea, mild vomiting, general malaise, and slight cyanosis. Treatment should not be curtailed or interrupted on account of these milder toxic effects.

Severe toxic effects include marked and persistent cyanosis, pallor, persistent dyspnoea, skin reactions, diarrhoea, hyperpyrexia or subnormal temperature, peripheral neuritis, optic neuritis, and severe prostration. The most serious effects are severe blood disorders with or without jaundice, such as leucopenia, agranulocytosis, and haemolytic anaemia. Severe toxic effects are comparatively rare and are probably due to an idiosyncrasy to the drug; some patients have taken as much as 2.5 g. of the drug daily over a period of months without ill effects, while in others severe reactions have quickly followed the ingestion of small doses. The more important toxic reactions will be considered in detail.

Cyanosis

Cyanosis is the most common toxic reaction, occurring in some degree in about 75 per cent of patients taking the drug. It is not necessarily associated with a change in the blood pigment, and, in such cases, may possibly be due to the formation of a pigment in the tissues derived from the drug itself. In more severe cases the blood has been found to contain large quantities of sulphaemoglobin or methaemoglobin, or rarely both. Neither substance has been found to cause any serious effects. Sulphaemoglobinaemia results from a combination of sulphuretted hydrogen from the intestine with haemoglobin, sulphanilamide acting as a catalyst. The condition can be largely prevented by avoiding the use of purgatives, such as magnesium sulphate, which produce liquid stools and thus encourage formation of H_2S , and by giving a low-residue diet from which eggs or other sulphur-containing foods are excluded. Cyanosis, unless severe, should not contra-indicate continuance with the drug.

Hyperpyrexia

A rise in temperature, reaching as high as $102^{\circ}F.$, may occur within 7 to 14 days of institution of sulphonamide therapy, and may be mistaken for a recrudescence of the original infection. Garrod suggested that this pyrexia might be due to liberation of the products of lysed bacteria. The temperature falls as soon as the drug is withheld.

Skin reactions

A variety of types of skin reaction has been described following the use of sulphonamide drugs. These may be morbilliform, scarlatiniform, purpuric, maculo-papular, or urticarial, and may be generalized or patchy in distribution. In rare cases exfoliative dermatitis has occurred. Rashes most commonly occur on parts of the body exposed to sunlight, and various reports of their occurrence in patients receiving ultra-violet irradiation while they were taking a sulphonamide compound have appeared. Rimington and Hemmings showed that sulphanilamide causes an increased excretion of porphyrins in the urine, and of these coproporphyrin I is an active photo-sensitizer. This led them to

suggest that photo-sensitization is the cause of these skin reactions. With derivatives such as M & B 693, in which the amide group is substituted, porphyrins are not excreted.

Various other theories have been advanced to explain the occurrence of these rashes. These include allergy, a toxic result of failure to eliminate properly the drug, and the liberation of toxins by the drug from some hidden focus of infection (Erskine).

Nervous system

Peripheral neuritis, paraesthesia, and paresis have been reported in a few cases, especially after the use of uleron. Roch *et al.* reported a case in which the symptoms simulated amyotrophic lateral sclerosis.

Agranulocytosis

The most serious toxic reaction is agranulocytosis. Fortunately the condition is rare, though slight degrees of lymphocytopenia are comparatively common. The symptoms due to the condition are indefinite, consisting of pyrexia, severe headache, and deterioration in the general state of the patient, and a diagnosis can only be made by means of a blood count. In view of this a blood count should be made at least every third day in patients who have been receiving sulphonamide drugs for more than ten days. The occurrence of agranulocytosis appears to be as common with M & B 693 as with sulphanilamide.

Haemolytic anaemia

Haemolytic anaemia, which is also a rare toxic effect, occurs within the first few days of treatment with sulphonamide compounds. It is characterized by a sudden fall in the number of red blood-cells, and is associated with some jaundice and haematuria. The resumption of the drug after a period of rest is not followed by recurrence.

DOSAGE

Since, with a constant dosage of the drug, patients reach an equilibrium between intake and output in 2 to 3 days it is generally possible, by adjusting the dosage, to keep the blood concentration at any desired level. The total daily dosage and the frequency of giving individual doses depend necessarily on the patient and on the disease. For the treatment of severe infections with sulphanilamide, a concentration of 10 mg. per 100 c.cm. is necessary, and this is generally obtained by a daily dosage of 1 g. (15 grains) for every 20 lb. of body weight (an average daily dose for an adult is 120 to 150 grains). As a rule the drug should be given every 4 hours in order to maintain the optimal blood concentration. In milder infections it is advisable to avoid too high an initial dosage, and to increase the dosage gradually over a period of 2 days until a blood concentration of 5 to 6 mg. per 100 c.cm. is reached.

To avoid possible toxic effects, a high dosage should not be maintained for a longer period than is necessary to effect clinical improvement. At the same time the dosage should be reduced gradually, since too rapid a withdrawal of the drug may allow of a relapse which may be uncontrollable by resumed administration. With a view to preventing acidosis, 0.5 to 1 g. of sodium bicarbonate may be given with each dose of sulphanilamide. The scale of dosage for M & B 693 is similar to that of sulphanilamide.

In treating urinary infections, high concentrations of the drug in the urine are more important than high blood concentrations. Smaller individual doses of about 5 to 15 grains, given 3 or 4 times a day, with restriction of fluids, will usually produce sufficient urinary concentrations of the drug.

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PART III
ABSTRACTS
OF MEDICAL LITERATURE

ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES

See also Vol I, p. I and Cumulative Supplement, Key Nos. 1-11.

Diagnosis

In a large group of cases C. Lintgen and K. Fry found that the determination of the sedimentation rate was of no value in the differential diagnosis between acute appendicitis and acute pelvic inflammatory disease; 10 per cent of the patients with acute pelvic inflammatory disease and 48 per cent of those with acute appendicitis had a normal sedimentation rate. All the cases were comparable as regards the extent of morbid changes and the duration of symptoms.

C. H. Osborn describes a method for diminishing that voluntary contraction of the abdominal musculature which is observed in nervous and apprehensive patients. It is argued that the orthodox position in which the patient is lying on the couch with the head and neck elevated by a pillow and the hip and knee joint semiflexed does not obliterate the lumbar lordosis, and that to accomplish this, when the patient has been placed in the orthodox position with the knees drawn up and the feet firmly placed, he should be asked 'to raise his tail bone one inch, from the couch'. This position can be maintained with ease. The superior relaxation is achieved mainly by contraction of the hamstring group of muscles and of the ischio-femoral part of the adductor magnus, assisted by the posterior part of the gluteal muscles.

P. W. Brown reported 3 cases of pain in the groin and thigh of a very distressing character, puzzling in diagnosis, and of grave prognostic significance, occasionally complicating intestinal disease, such as diverticulitis. It was attributed to perforation of the intestine causing a deep-seated abscess in the region of the psoas muscle.

J. E. Spalding and S. H. Wass published 2 case reports of spontaneous pneumoperitoneum, in each of which the outstanding symptoms were sudden pains in the epigastrium associated with acute pain in the right shoulder. A leaking ulcer was diagnosed in each case. Pain referred from the diaphragmatic distribution of the phrenic nerves to the area of skin served by the supraclavicular nerves occurs commonly after gastric and duodenal perforation, after rupture of the spleen, and when there is subdiaphragmatic suppuration. This pain is generally believed to be due to irritation of the sensory fibres of the phrenic nerve by the gastric contents or by blood or pus. As an alternative to explain the present cases it is suggested that the presence of air below the diaphragm allowed the liver to drop, the authors suggested that the liver is usually held in position by a thin layer of fluid between it and the diaphragm, and that the weight of the liver being thus concentrated on the small area of the diaphragmatic attachment of the suspensory ligament resulted in stimulation of the phrenic nerve.

Brown, P. W. (1939) *Proc. Mayo Clin.*, **14**, 404.

Lintgen, C., and Fry, K. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 393.

Osborn, C. H. (1939) *Brit. med J.*, **1**, 1086.

Spalding, J. E., and Wass, S. H. (1938) *Guy's Hosp. Rep.*, **88**, 440.

Treatment

Use of Splanchnic Anaesthesia

R. Liotier reported on the use in over 60 cases of splanchnic anaesthesia in certain abdominal conditions both for diagnostic and for therapeutic purposes. The technique used was a modification of that described by Kappis and Roussel, i.e. without laparotomy. A fine and rigid needle 10 inches long was used and 20 to 40 c.cm. of 0.5 to 1.0 per cent syncaine (procaine hydrochloride) were injected. The site of injection was 3 finger-breadths from the spinous process below the 12th thoracic vertebra, and the needle was pushed in obliquely towards the T_{xii} or L_i vertebral body. At a depth of 3 or 4 inches bony contact was usually made with the vertebral body, and the needle pushed further in front by being guided by the relation to the vertebra. The injection was only made when no effort was necessary to press the plunger, as the observance of this precaution ensured injection into the soft tissue around the coeliac ganglion. The author recorded only 3 complications, all of which concerned puncture

of the theca. After explaining the technique of the procedure the author expressed the view, based on his clinical material, that this method not only stopped pain most effectively in almost any intraperitoneal and extraperitoneal condition in the abdomen (excluding organic obstruction) but that it was a valuable aid in differentiating functional or spasmodic conditions from mechanical ileus. Among the painful conditions successfully treated by anaesthesia of the coeliac ganglion the author described intestinal colic due to ulceration, subperitoneal cellulitis, peritonitis due to perforated gastric ulcers, functional coeliacgia, lead colic, hepatic colic, renal colic, and renal pain due to hydronephrosis and wandering kidney. The method was also successful in treating anuria due to calculi, and also secured the safe and painless passage of the stone, while its effect on ureteral spasms was most remarkable. In a case of chronic pancreatitis with spasms and icterus the splanchnic infiltration relieved the pain and the spastic phenomena. Functional ileus was also improved and the author concluded by recommending the method for further trial especially with regard to the elimination of its masking effects in abdominal emergencies.

Liotier, R. (1939) *Rev. Chu., Paris*, **58**, 385.

ABORTION

See also Vol. I, p. 47, Cumulative Supplement, Key No. 12; and p. 30 of this volume.

Medical Grounds for Abortion

B. Solomons stated the conditions under which he considered it was justifiable to kill a fertilized ovum or a viable foetus. Dealing with problems of general health, he stated that the pregnancy might be terminated to save the mother's life or to safeguard her health. During the first 28 weeks of pregnancy, severe toxæmia and hyperemesis gravidarum which do not respond to treatment call for abortion which should not be delayed too long. Solomons recommended curettage in the first 3 months and vaginal or abdominal hysterotomy later in pregnancy. Renal toxæmia can usually be treated sufficiently to enable the pregnancy to continue.

Should hæmorrhage occur during this period and the foetus die, the ovum should be removed by the usual methods. Solomons considered that the victim of uncompensated cardiac disease should not be allowed to become pregnant but, if this occurred, it might be necessary to induce during the first 3 months, or if she came to term, her labour should be helped with sedatives and forceps. He thought that Caesarean section was not the method of choice in this condition or in tuberculosis as many patients died 2 or 3 weeks after operation. If severe toxic goitre occurred in the first 3 months, it could nearly always be treated with sufficient success for the patient to go to term.

During the last 3 months of pregnancy the conditions calling for interference, which are most commonly encountered, are disproportion and inertia. Solomons stated emphatically that it was never necessary to perform a craniotomy on a live child, for, in cases of disproportion, a lower segment Caesarean section, with drainage if necessary, can be carried out with safety even in cases in which there has been some manipulation.

To avoid foetal death in cases of inertia, he stressed the importance of knowing exactly when to interfere in the case. When the temperature or pulse begins to rise and the foetus to show signs of distress, lower segment section with drainage must be considered. Vaginal delivery should not be attempted unless the head is well down and the cervix three-quarters dilated. Dealing with the use of Caesarean section and drugs during labour, the author stated that they should be used with discretion. It is safest to delay giving pituitary extract until the placenta is out, and in using quinine the danger to the foetus should be borne in mind.

Considering the question of destroying monsters Solomons stated that each case should be considered on its own merits. It may be necessary, as in hydrocephalic foetuses, to destroy the child to effect delivery.

Solomons, B. (1939) *Brit. med. J.*, **1**, 1175.

Complications

Three fatal cases of infection with *Cl. welchii* following abortion are described by R. Y. Dawbarn and B. Williams. In 2 of these the infection was fulminating and the

main feature was the occurrence of haemolysis. Death occurred in 19 and 21 hours respectively from the onset of symptoms. The condition was attributed to shock or chemical poisoning, a correct diagnosis not being made before death. In the third case, which also proved fatal, gas was present in the vaginal loss and the smears contained organisms morphologically similar to *Cl. welchii*. *Cl. welchii* was absent from blood cultures taken during life, and haemolysis was almost completely absent at necropsy. In none of the 3 cases was the mode of infection determined, but all patients admitted having taken drugs to procure abortion.

Dawbarn, R. Y., and Williams, B. (1938) *Brit. med. J.*, **2**, 279.

ABORTUS FEVER

See also Vol. I, p. 68 and Cumulative Supplement, Key No. 13.

Morbid Anatomy

R. M. Calder *et al.* investigated the blood of nearly 300 patients suffering from brucellosis. They found changes which, taken together, they concluded were specific for the infection. The changes occurred both in patients having agglutinins and opsonins in addition to a positive skin reaction and in those who had only a positive skin reaction. A lymphocytosis, with an absolute increase in the number of lymphocytes and an increase in the number of immature lymphocytes, was found. The erythrocyte counts were approximately half a million below normal, the anaemia being of the macrocytic or hypochromic type. Blood coagulation was slow and sometimes not complete and clot retraction was often imperfect. Eosinophilia occurred in about one-fifth of the cases and plasma cells were often encountered.

Calder, R. M., Steen, C., and Baker, L. (1939) *J. Amer. med. Ass.*, **112**, 1893

Treatment

H. Welch *et al.* investigated the effect of sulphanilamide on the opsono-cytophagic activity of patients suffering from brucellosis. They reported 5 cases in which it was increased. In 3 of the cases there was no agglutination with *Brucella* until after the therapy began, when agglutinins appeared. In suspected cases this fact was valuable in diagnosis. Eleven guinea-pigs infected with *Brucella abortus* and treated with sulphanilamide all showed an increase in phagocytosis and a raised opsonic index. Examination of the animal blood showed that after treatment the leucocytes began to engulf the organisms, and there appeared to be a positive chemotaxis of the organisms for the white cells. In a control untreated group, no increase in the opsonic index was seen.

A. P. Thomson treated 2 cases of abortus fever with foudadin and 3 with prontosil; a special feature of the 2 latter was the decline in the specific agglutinations to negligible titres. Both treatments were regarded as of value and prontosil may prove to be a simple specific remedy if the patient can tolerate it in moderate doses (3 g. daily) for a week.

Thomson, A. P. (1938) *Brit. med. J.*, **2**, 884.

Welch, H., Wentworth, J. A., and Mickle, F. E. (1938) *J. Amer. med. Ass.*, **111**, 226.

ACCESSORY SINUSES OF THE NOSE

See also Vol. I, p. 77.

Anatomy

C. M. Anderson comments on the rarity of congenital occlusion of the choana. At the Royal Infirmary, Edinburgh, only 6 cases occurred out of 27,863 attending the Ear, Nose and Throat Department, and only 160 cases have been reported in the last hundred years.

The author discusses 6 cases which had been dealt with at the Mayo Clinic, and he considers that more cases would be found if the condition were recognized more

often in infants with nasal obstruction. The symptoms may be confused with those resulting from an enlarged thymus. He says that an individual may grow to full maturity in relatively good health without a nose, or with only half a nose, respiratory functions being taken over by the mouth. Most of the patients have no ear symptoms, and other developmental abnormalities are relatively infrequent. Some defect in speech, however, is usual. The obstruction can be permanently relieved by surgical means. The type of treatment should be determined by the needs of the particular case.

Anderson, C. M. (1937) *J. Amer. med. Ass.*, **109**, 1788.

Treatment

P. R. Cannon and T. E. Walsh warn against the wide-spread and indiscriminate use of oily nasal sprays, particularly in infants. The smoothness of the mineral oil, and possibly the mild anaesthetic effect of the menthol which is often contained in the spray, make it gravitate from the nasopharynx to the trachea without eliciting the cough reflex, or stimulating reflex closure of the epiglottis. The passage of the oil into the lungs is particularly liable to occur with infants lying on their backs, and the authors consider that this is probably one cause of lipid pneumonia.

They also give a warning against this use of silver protein and similar solutions as nasal antiseptics. Although these are advertised as 'non-irritating and non-toxic', Cannon and Walsh found, by experimental work on rabbits, that this form of nasal medication was followed by pulmonary oedema, necrosis, haemorrhage, and focal broncho-pneumonia.

Other materials used as a protection against the entrance of the virus of poliomyelitis from the nose to the brain, such as astringent sprays of zinc sulphate, picric acid, and tannic acid, are also, in their opinion, a possible source of danger.

S. N. Parkinson makes suggestions for the local treatment of infections of the upper part of the respiratory tract to improve drainage: (i) The head-low posture advocated by Proetz. The patient is supine with the head extended. The posture presented is that in which the head is inverted laterally. He lies on his side with his head bent downward exactly sidewise, using the shoulder as a fulcrum. (ii) Preliminary shrinkage of the nasal mucosa is first obtained by the use of ephedrine solution in an atomizer, this may take 5 to 10 minutes. The patient is then placed in the lateral head-low posture, and a solution of ephedrine is instilled into both nasal chambers. After from 3 to 4 minutes the head is rotated to face downward in order to permit the nasal contents to escape from the nostrils. This posture has been advocated on the grounds that it renders available all important structures within the nose, and permits of treatment that is entirely free from trauma. Benzedrine may be used as an alternative.

Cannon, P. R., and Walsh, T. L. (1938) *New int. Clin.*, 1st ser., **3**, 109.

Parkinson, S. N. (1939) *J. Amer. med. Ass.*, **112**, 204.

Tumours of the Accessory Sinuses

A. G. Rawlins found that osteomas of the maxillary sinus are benign and do not invade the surrounding tissues or metastasize, but they do displace and erode the surrounding tissues. The disease is rare; the 27 cases so far published are reviewed by Rawlins, and 2 more are reported. The tumours are hard irregular masses which may reach a great size and erode the skin or intracranial structures. Trauma appears to be the most likely aetiological factor. Suppuration of the antrum is common, and neuralgia may be present if the tumour presses on the infraorbital nerve. Exophthalmos may occur from pressure on the eyeball, and impaired vision from pressure on the optic nerve. Swelling of the cheek may occur, but the anterior and lower walls of the antrum are more resistant to pressure than are the upper and inner walls. The diagnosis is best confirmed by X-ray examination. Treatment of the condition is surgical, care being taken to remove the pedicle and the bone from which the pedicle arises; if this is not done there will be recurrences. The mortality-rate in this series was 8.7 per cent in the operated cases, and 40 per cent in the non-operated. There was a history of injury in 20 per cent and of sinus infection in 28 per cent. Five of the tumours were dead osteomas.

Rawlins, A. G. (1938) *Ann. Otol. etc., St. Louis*, **47**, 735.

ACHALASIA

See also Vol. I, p. 116 and Cumulative Supplement, Key No. 18.

Of the Pharyngo-Oesophageal Sphincter (Plummer-Vinson Syndrome)*Course and Prognosis*

Carcinoma may occur in irritated tissue (such as the mouth and pharynx of men, tobacco and alcohol presumably acting as irritants), in tissue the subject of chronic inflammation, and in atrophic tissue. L. Johnson gave an example of the last in a woman who developed a post-cricoid tumour after having suffered from anaemia and the Plummer-Vinson syndrome. Dysphagia is a part of this syndrome and the mucosa shows morbid changes. The Plummer-Vinson syndrome occurs much more commonly in women than in men, and 90 per cent of post-cricoid carcinomas occur in women. The syndrome is most commonly present from 15 to 20 years of age and never appears after 50. Carcinoma may follow much later, and the author suggests that its later appearance may be due to this alteration of the oesophageal mucosa in earlier life.

Johnson, L. (1938) *Ann. Otol., etc., St. Louis*, **47**, 809.

ACHLORHYDRIA

See also Vol. I, p. 126 and Cumulative Supplement, Key No. 19.

Aetiology

S. Morrison discusses achylia as associated with gastritis and carcinoma of the stomach or with pernicious anaemia. He believes that the pylorus possesses a hormone which acts like secretin and stimulates the oxyntic cell to secrete antianæmic factor. The effect of the pituitary gland and pituitary preparations on the oxyntic cells is discussed. Neutral red will detect more minutely than any other test whether the gastric mucous membrane has latent secretory and excretory possibilities. Further, it gives information concerning the oxyntic or parietal cell activity.

The author thinks that the pyloro-duodenal mucosa may elaborate a hormone which stimulates the secretion of the intrinsic factor of Castle by the gastric glands. The latter acts on food materials to produce substances preventing pernicious anaemia. It is pointed out that pernicious anaemia may possibly be curable if the treatment consists in the stimulation of pyloric gland activity, which in turn provides a stimulus to the oxyntic cells to secrete that intrinsic factor. Such therapy may include the temporary administration of pyloric gland powder. The author makes it clear that much of the work is still experimental. The pepsin hypothesis postulates that pepsin is secreted mainly, if not entirely, by the fundus of the stomach, and may antagonize the intrinsic factor potency of the fundus. The hypothesis of a pyloro-duodenal hormone is supported by two demonstrations: (i) the close functional and anatomical inter-relationship of the pylorus and duodenum; (ii) if depepsinized fundus substance is potent in pernicious anaemia, then its mechanism of action differs from that of depepsinized pylorus substance.

Morrison, S. (1938) *Amer. J. digest. Dis.*, **5**, 617.

ACNE

See also Vol. I, p. 156.

Treatment*Local*

Cryotherapy.—F. L. Karp *et al.* treated 50 cases of acne and the resultant scarring by cryotherapy, good results being obtained in 47 cases. Two patients did not respond to treatment and one suffered a recurrence. A paste was prepared of solid carbon dioxide, acetone, and precipitated sulphur. Application to the skin was made by means of gauze, and the paste allowed to remain on for 20 minutes. After removal, erythema and slight oedema were apparent, and mild exfoliation of the epidermis followed 2 or 3 days later. The therapeutic response was considered to be due to

repeated exfoliations. The treatment was found of use in fresh cases, and in some which had been unsuccessfully treated with X-ray therapy. Good cosmetic results were obtained in cases previously cured by irradiation, and it was found that the acne of puberty responded well. The average length of time of treatment in two-thirds of the cases was 4 months.

Endocrine

Considering that acne vulgaris is associated with the development of the sexual function, I. D. Riley carried out treatment with testosterone propionate in 20 cases, and instituted a further series of 10 controls. The controls were given 0.5 c.c. of distilled water subcutaneously each month, and the testosterone was given weekly in increasing doses up to 50 mg. per week for 3 months, the average total dosage in that time being 300 mg.

The results were not dramatic as in many cases of X-ray therapy, but in mild cases the acne papules often cleared up and left only stains. Severe cases and those which had previously received X-ray therapy did not respond. These results were not sufficiently remarkable to suggest the adoption of this measure as an official treatment.

Tuberculin

M. T. Van Studdiford performed tuberculin tests on 49 cases of acneiform eruptions which did not respond to the usual methods of treatment, and followed these tests with therapeutic administration of tuberculin. The tests were made with old tuberculin (Koch) in dilutions varying from 1:100,000 to 1:1,000. Of 25 patients (24 positive to human or bovine, or both, and 1 negative to both) treated for 60 days or more with old tuberculin, 10 were cured and 11 improved; the remaining 4 were not included in the report because of the short time they had been under treatment. Tuberculin gives good results in the treatment of tuberculoderma and, used with care, has cleared up long-standing acneiform lesions without any undesirable complications.

Karp, F. L., Nieman, H. A., and Lerner, C. (1939) *Arch. Derm. Syph.*, N.Y., **39**, 995.

Riley, I. D. (1939) *Brit. J. Derm.*, **51**, 119.

Van Studdiford, M. T. (1938) *Arch. Derm. Syph.*, N.Y., **38**, 737.

ACTINOMYCOSIS

See also Vol. I, p. 173 and Cumulative Supplement, Key No. 26.

Treatment

Sulphanilamide.—L. M. Miller and E. H. Fell report a case of abdominal actinomycosis in a boy of 11 which was cured by sulphanilamide therapy. There was a tender inflammatory mass, the size of an apple, lying midway between the umbilicus and symphysis, a leucocytosis of 14,000, and a marked pyrexia. Catheterization brought about no reduction in the size of the swelling. Following the application of hot fomentations, reddening of the skin, the development of fluctuation, and a spontaneous opening at the umbilicus, an incision to ensure better drainage was made 11 days later over the centre of the mass, and copious thick pus was evacuated. The wall was thick and the nature of the discharge suggested actinomycosis. The diagnosis was confirmed by the presence microscopically of the typical granules. No improvement, but a gradual deterioration, resulted from the use of 7 grains of thymol and potassium iodide given once each day, and accompanied by 16 X-ray applications at intervals of 4 to 6 days over a period of 4 months. The administration of sulphanilamide, 10 grains 3 times a day, in addition to the other medication brought about a rapid improvement within one week. Within 2 months the boy was discharged from hospital having gained 10 lb. in weight and with the abdominal mass much reduced in size and giving little drainage. The subsequent history was entirely satisfactory.

Thymol.—F. W. Bancroft and M. Stanley-Brown analysed 500 cases of actinomycosis, and found that 20 per cent were abdominal. They discussed the treatment introduced by H. B. Myers, who advised adequate surgical drainage and packing with 10 to 25 per cent thymol in olive oil, and tolerance doses of the crystals by mouth, to prevent the spread of the disease to other parts.

The authors review the result of this treatment in a case of actinomycosis of the crest of the ilium following appendicectomy. Large doses of potassium iodide had been tried, but without effect. Constant pain, and the poor condition of the patient, led them to try Myers' method. This resulted in a considerable amount of healing, a speedy improvement in the pyrexia, and a gain in weight of 37 lb. A. O. Whipple, in the discussion following this paper, states that thymol undoubtedly has a real place in the therapy of this condition, but he stated that some patients are quite intolerant of the large doses employed.

Bancroft, F. W., and Stanley-Brown, M. (1938) *Ann. Surg.*, **108**, 468.

Miller, E. M., and Fell, E. H. (1939) *J. Amer. med. Ass.*, **112**, 731.

ACTINOTHERAPY

See also Vol. I, p 180 and Cumulative Supplement, Key No. 27.

Physiology

Bactericidal Power

D. Hart and P. W. Sanger stated that ultra-violet irradiation of an intensity of 28 to 30 microwatts per sq. cm. could, in less than 5 minutes, sterilize between 95 and 100 per cent of *Staphylococcus aureus* and other organisms on a petri dish of blood agar. With this apparatus, over 80 per cent of the output was at 2,537 Angstrom units. It also reduced by 95 per cent the number of viable organisms dropping from the air. They experimented to find the effect of this bactericidal irradiation on the wounds of animals, using it to sterilize the air in the operating field. They found that the wounds healed as well and sometimes better than control wounds. Exposure of the peritoneum to this irradiation, sometimes for 30 to 90 minutes, produced no morbid changes. In 1,000 patients exposed to this irradiation, the wounds healed more quickly with less infection and less systemic reaction. It is necessary to protect the eyes and skin of the surgeon, assistants, and staff from the effects of the irradiation.

D. Hart *et al.* exposed cultures of organisms and fungi to ultra-violet radiation of 2,537 Angstrom units at an intensity of 28 to 30 microwatts per sq. cm. The exposure was made at a distance of 5 feet, that is at the distance from the operative site that the tubes are mounted in the operating theatre, when used to sterilize the wound and the air surrounding it. Most of the bacteria were killed in 3 minutes, but the fungi were more resistant, possibly due to their tendency to grow in clumps. Owing to its effective bactericidal power Hart and his co-workers considered that this method was valuable in securing an aseptic surgical technique.

Hart, D., and Sanger, P. W. (1939) *Arch. Surg., Chicago*, **38**, 797.

-- Devine, J. W., and Martin, D. W. (1939) *ibid*, **38**, 806.

ADENOIDS

See also Vol. I, p. 193.

Treatment

X-Irradiation

R. Clément *et al.* reported on the use of radiotherapy in the treatment of adenoid hyperplasia in infants and in children. Adenoid hyperplasia had a relation to the pituitary, and a course of radiotherapy, by reducing the lymphoid tissue in size and inhibiting its hypersecretion, was thought by the authors to be more effective than surgical treatment. The technique adopted was to irradiate in a plane which centred around the mandible; the eyes were protected by lead-covered glasses. The second plane of irradiation was from the side on the auricular and zygomatic region; in certain cases a third field also was chosen, centring the rays on the nose. A distance of 28 cm. was constantly employed, and 0.5 mm. copper, 1 mm. aluminium, and 1 cm. of wood were used for screening. A total of 360 to 600 r were irradiated in each field in 3 sittings, according to age and clinical symptoms. No accidents or side-effects occurred with this method. The authors' results showed improvement in two-thirds of all cases.

Clément, R., Gilbert, P., and Clénet, E. (1939) *Pr. méd*, **47**, 786.

ADIPOSIITY

See also Vol. I, p. 202.

Clinical Picture

Genito-Pituitary Adiposity

On the basis of investigation of 16 boys between the ages of 4 and 14 years, B. Mittelmann describes a form of juvenile adiposo-genital dystrophy which, though presenting in a mild form most of the features of Fröhlich's disease, differs from it in some respects. In the first place it is curable, either spontaneously or as the result of injection of extract of pregnancy urine. There is no evidence of an intracranial expanding lesion, such as a tumour or hydrocephalus, or any history of encephalitis. No necropsy is on record, but the success of treatment by extract of pregnancy urine suggests that there is an anterior pituitary deficiency. The neurological symptoms may be limited to hypotonia or include intention tremor, spasmodic torticollis, and nystagmus. The psychopathological manifestations, studied in detail, are chiefly depression, over-subservience, over-dependence, and over-aggressive hostile behaviour disturbance.

Dercum's Disease

R. Boller described the 4 symptoms of Dercum's disease (i) Adiposity mainly involved the lower parts of the body, but in a few cases the arms, shoulders, and breasts were also affected. The surface of the fatty masses was uneven, soft in some areas and hard in others. The skin over the adipose areas was hyperaesthetic. (ii) Pain on pressure in the affected parts had been observed even before the deposition of fat; the hard nodular parts of fat were the most painful. An important point in the differential diagnosis was hyperaesthesia of the fatty tumours and of the skin; in its absence the condition was probably a lipomatosis and not Dercum's disease. Spontaneous pain varied in degree, being more severe when the patient moved about. Pain on pressure was of diagnostic importance only when combined with spontaneous pain, because fat tissue in most other cases of adiposity is also sensitive. There was not any difference in the chemical composition of normal fat and fat in Dercum's disease. (iii) Muscular weakness: the irritability of the muscles to electrical stimuli in Dercum's disease was normal. It had therefore been suggested that the muscular weakness was due to pain; the pain was sometimes so severe that it was not relieved by morphine. (iv) Psychic changes included nervous irritability, dementia, and depressive conditions; in most cases there were insomnia, vertigo, headache, psychic lability, and neurasthenia. Most of the psychic changes are probably caused by the pain and the difficulty of moving. Little was known about the aetiology of Dercum's disease (e.g. alcoholism and syphilis) and the morbid anatomy did not show any peculiar findings. Dercum's disease was regarded as an adiposity of unknown origin with a polyneuritis in connexion with the lipomas.

Treatment—Various endocrine preparations, thyroid and pituitary, had been recommended in treatment but with little effect. Novocain infiltration was recommended: a sterile solution (0.2 to 0.4 per cent) of novocain (procaine hydrochloride) with addition of 0.4 per cent sodium chloride was injected into the most painful parts of the fat in doses of 10 c.cm. increasing by 10 c.cm. to 60 c.cm., 2 or 3 injections being made into the various parts of the body; if injected deeply this at once relieved the pain which did not return. Penetration of the skin by the needle was extremely painful. The adiposity was not influenced by this treatment. Treatment of the heart by digitalis and diuretics should accompany the treatment of pain. Dietetic treatment of the adiposity was also recommended.

Boller, R. (1939) *Med. Welt*, **13**, 329.

Mittelmann, B. (1938) *Endocrinology*, **23**, 637.

Treatment

Dinitrophenol.—W. E. Borley and M. L. Tainter investigated the problem of any causal relation between dinitrophenol medication, often employed for weight reduction, and cataract formation. In feeding experiments lasting up to 6 months each, white rats were given lactose-containing diets, which usually produced cataracts. One half of the rats received 0.075 per cent *alpha*-dinitrophenol in addition. The eye of each rat was examined ophthalmoscopically and with a slit-lamp

at frequent intervals. No cataracts were produced on a 25 per cent lactose diet whether or not dinitrophenol was administered. On diets containing 50, 60, and 70 per cent lactose the majority of rats showed cataractous changes, the degree of change being proportional to the lactose percentage in the diet. At the 70 per cent level the cataracts became mature, and finally liquefied. Addition of dinitrophenol to these cataract-producing diets did not alter the frequency of appearance of the cataracts, their rate of progress, or the extent of the changes. The general conclusion was that dinitrophenol therapy for weight reduction did not predispose to cataract formation.

Metabolism-stimulating hormone.—A metabolism-stimulating hormone (provisionally called No. 622) different from all the other hormones of the pituitary, except the melanophore substance of the pars intermedia, was isolated from both lobes and the pars intermedia of the pituitary by D. K. O'Donovan and J. B. Collip. The rise of the basal metabolism was largely at the expense of the fatty tissues. This metabolic effect has been shown to occur in man, and the use of this new metabolic stimulant is under trial by I. M. Rabinowitch *et al.* in the treatment of obesity and other conditions in which an increase of metabolism is desirable.

Diet.—R. Boller and W. Pilgerstorfer recommended for the treatment of adiposity the alternation of 2 diets. There are 2 ways of treating adiposity: to increase metabolism and to reduce the intake of food. Drugs, e g. thyroid, iodine, dinitrophenol, have mainly been used to increase the consumption (oxidation) of food, but all are prone to have toxic effects. It is very difficult to reduce food intake in an adipose person as close supervision is necessary and after treatment the patient will resume his previous diet and his weight will soon increase. Reduction of carbohydrates brings about a loss of weight but the organism becomes adapted to a low carbohydrate diet and, after 6 to 7 days, no more weight is lost. The diet advocated consisted of protein and fat for 5 days and of protein and carbohydrate for 3 days. During the 5 days of protein-fat diet there was a steady loss of weight, and during the following 3 days of protein-carbohydrate diet the weight previously lost was not regained. In 11 cases of obesity on the new diet there was an average daily loss of weight of 91 grams. It was necessary to keep most strictly to the diet; even a small piece of bread during the carbohydrate-free period might reduce the loss of weight. A list was given of the articles of food permitted and prohibited in each type of diet and a complete sample diet for 16 days was appended.

Boller, R., and Pilgerstorfer, W. (1938) *Z. klin. Med.*, **134**, 614.

Borley, W. E., and Tainter, M. L. (1938) *Amer. J. Ophthalm.*, **21**, 1091.

O'Donovan, D. K., and Collip, J. B. (1938) *Amer. J. Physiol.*, **123**, 157.

Rabinowitch, I. M., Mountford, M., O'Donovan, D. K., and Collip, J. B. (1939) *Canad. med. Ass. J.*, **40**, 105.

ADRENAL GLAND DISEASES

See also Vol. I, p. 232, Cumulative Supplement, Key No. 30; and pp. 109 and 166 of this volume.

Addison's Disease

Aetiology and Pathology

D. L. Mendel and M. Saibil of Montreal recorded a case of Addison's disease in a man, aged 30, with extensive bilateral pulmonary tuberculosis, emaciation, some scattered pigmentation over the shoulders, a systolic blood pressure of 88 and diastolic of 58 mm. Hg, albuminuria and pyuria, much abdominal pain, and asthenia. At the necropsy at the Mount Sinai Sanatorium, amyloid degeneration was found in the spleen, liver, kidneys, intestines, prostate, and adrenals. There was, in addition to pulmonary tuberculosis, a small tuberculous ulcer in the ileum (without perforation, which had been suspected before death). The adrenals did not show any tuberculous lesions. Amyloid disease of the adrenals is not uncommon in cases of generalized amyloidosis, but Addison's disease is very rarely associated without other lesions such as tuberculosis. Emphasis was laid on the rarity of Addison's disease in sanatoriums, shown by the 5 cases only reported among more than 7,000 sanatorium patients.

Metabolic Changes

W. Cramer and E. S. Horning found by a series of experiments on mice that (i) adrenalectomy is followed by changes in the thymus, the pituitary, and in the mamma which are the reverse of those produced by oestrinization; (ii) oestrinization renders mice resistant to adrenalectomy, as judged by their survival; and (iii) adrenalectomy makes mice resistant to the physiological effects of the oestrogenic hormone of the ovary. These facts led to the conclusion that the adrenal possesses hormonal functions which are synergic with the oestrogenic functions of the ovary. The pathological effect produced by the prolonged application of the ovarian oestrogenic hormone—carcinogenesis in the mamma—can also be weakened in the absence of the hormonal activity of the adrenal glands. It follows that the adrenal possesses hormonal functions which play a part in the aetiology of mammary cancer.

A. D. Marenzi found that adrenalectomy in dogs produced a decrease of sodium and chloride and an increase of potassium and phosphorus in the plasma: cortical extract restored these to normal. Potassium injections produced a greater and more lasting increase in blood potassium in adrenalectomized than in normal dogs. Extirpation of the sympathetic abdominal chain and splanchnic nerves did not modify the plasma potassium. Demedullation of one adrenal and extirpation of the other produced no immediate change in the plasma potassium, but 6 to 13 days later there was a slight increase attributed to a mild degree of adrenal insufficiency. Marenzi suggested that two factors were involved in these changes: (i) The adrenal cortical hormone, which regulates the fixation of potassium by the tissues, the excretion by the kidney, and the equilibrium between plasma and tissue potassium, all of which are disturbed by removal of the adrenal gland, and (ii) adrenaline, which effects the rapid mobilization of liver potassium.

Treatment

Cortical hormone.—The effect of a single subcutaneous injection of adrenal cortical extract is short-lived, and a constant supply of the hormone can be maintained only by repeated injections. This is a serious disadvantage in the treatment of advanced Addison's disease. G. W. Thorn *et al.* found that a glycerin extract of adrenal cortex given by mouth prevented the usual sodium and chloride diuresis which follows bilateral adrenalectomy in dogs and maintained the dogs in healthy condition for long periods. Five cases of Addison's disease were successfully maintained on the glycerin extract; the ratio of the dose given twice daily by mouth to that given twice daily by injection was approximately 2.5 : 1. The extract was found unsuitable for the treatment of an acute crisis in Addison's disease, for which it is suggested that the hormone must be given parenterally.

W. O. Thompson *et al.* treated 7 patients with Addison's disease by prolonged injections of cortical extracts of the adrenals in high doses. Four of the patients were living after being under treatment for 1 to 3½ years. The preparation used was an extract made in the Wilson laboratories, 10 to 20 c.cm. being given daily. Larger quantities were necessary during infections and when the characteristic crises of the disease occurred. Early in a crisis the extract alone was effective, but later in the crisis, the patient being depleted of common salt, this must be given in addition to the extract. Treatment by mouth was tried on 2 women, but without much effect. If the basal metabolic rate is low, it should be raised to normal by thyroid extract. Provided that there is not active tuberculosis, prolonged treatment with large doses of the cortical extract should keep patients in a satisfactory state.

S. Thaddea summarized his observations on the relation of specific hormone therapy and the blood pressure in Addison's disease. Hormone therapy does not increase blood pressure in compensated cases, but in decompensated cases causes an increase of blood pressure. In Addison's disease there is a faulty regulation of the blood pressure and absence of the adrenaline blood-pressure reaction. Cortical hormone or cystein corrects these disturbances.

F. A. Hartman *et al.* have produced in animals a refractory state to adrenal extracts. After continued intravenous injections the animals became refractory to the type of extract used (beef) but still responded to pig, sheep, or horse extract. Subcutaneous injections failed to produce a refractory state, but intraperitoneal injections in the 2 animals tested appeared to have the same effect as intravenous.

H. W. Dryerre attempted to assess experimentally the value of standard cortical extract, cortin, and of desoxycorticosterone acetate in Addison's disease. The latter was available in two forms: (i) in tablets each containing 50 mg.; (ii) in solution in arachis oil: the concentration in this case was 5 mg. per c.cm. The patient selected,

a man aged 23, had required intensive treatment for Addison's disease in the last 4 years. The first 5 tests were concerned with a study of the influence of cortin on sodium and chlorine excretion. It caused a definite diminution of the sodium concentration in the urine. Desoxycorticosterone acetate reduced the sodium and chlorine in the urine of patients suffering from Addison's disease and greatly benefited their general condition. It was most strikingly effective when 200 mg. were implanted into the muscles of the anterior abdominal wall, since its action when injected proved much more temporary. Those cases of Addison's disease which are due to a simple atrophy of the adrenal gland respond well to this tablet implantation, but the more common variety, which is tuberculous, fails to react.

Diet.—E. H. Ryncarson, after a reference to the increasing frequency of reported cases of Addison's disease due to adrenal atrophy, vouched for the efficacy of a diet restricted in potassium by (i) limiting the selection of bread, cereals, and sugars to the highly refined products; (ii) the moderate curtailment of milk, meat, fruit, vegetables, and condiments; and (iii) the cooking of meat and vegetables according to the following special method—the vegetables are cut into small pieces and cooked in about 8 times their volume of water, thus reducing the potassium by 60 to 70 per cent without a concurrent diminution of palatability; meat is also divided into small pieces and cooked in a so-called parchment bag with from 6 to 8 times its volume of water. Foods to be avoided, because of a high potassium content, include soups, broths, and gravies containing meat stock or meat extracts, mustard, dried fruit, and vegetables, bran, and chocolate. Salt and white sugar can be used liberally. One litre of Addison's elixir (1 litre of water, 10 g. of sodium chloride, 5 g. of sodium citrate, and fruit extract as a flavouring) should be consumed daily.

Cramer, W., and Horning, E. S. (1939) *Lancet*, **1**, 192.

Dryerre, H. W. (1939) *Brit. med. J.*, **1**, 971.

Hartman, F. A., Lewis, L. A., and McConnell, K. P. (1939) *Endocrinology*, **24**, 197.

Marenzi, A. D. (1938) *Endocrinology*, **23**, 330.

Mendel, D. I., and Saibil, M. (1938) *Canad. med. Ass. J.*, **39**, 457.

Ryncarson, E. H. (1938) *J. Amer. med. Ass.*, **111**, 897.

Thaddea, S. (1939) *Endokrinologie*, **21**, 338.

Thompson, W. O., Thompson, P. K., Taylor, S. G., III, and Hoffmann, W. S. (1939) *Endocrinology*, **24**, 774.

Thorn, G. W., Emerson, K., and Eisenberg, H. (1938) *Endocrinology*, **23**, 403.

Hyperfunction of the Adrenal Cortex: Hyperplasia and Neoplasm

Clinical Picture

Adreno-genital syndrome.—C. Allen *et al.* described a case of paranoid schizophrenia associated with hirsutism from adreno-genital virilism, cured by unilateral adrenalectomy. The patient had a typical prepsychotic history and was always 'the odd one out' of the family. Hirsutism appeared at 14, and between 14 and 18 she twice suffered from writers' cramp and exophthalmic goitre. At the age of 24 she became religious, developed notions that she was unclean, and started to have ideas of reference and aural and olfactory hallucinations mainly referring to her foul odour and hirsutism. Her sexual history was devoid of any intense feelings, though she was strongly attached to a girl friend. Before operation, at the age of 34, she was grossly hallucinated with paranoid delusions of an unsystematized type. She made detailed notes of her own feelings, and in these frequently expressed the wish to urinate 'like a man standing up'. Following her operation she had a short attack of confusion, but otherwise made an uninterrupted recovery. The hair fell out, the signs of psychosis vanished, and she lost the desire to urinate like a man, though she did not develop any strong heterosexual desires.

The authors have previously shown that in the male foetus there is a phase of intense androgenic secretion from the 8th to the 20th week, while in the female the phase only lasts from the 11th to the 15th week. They suggested that bodily sex differences might be thus determined. It would appear that the female is, as it were, a 'suppressed male'. They suggest that, in the patient described, adrenal activity produced not only virilism but also intense intrapsychic conflict between biochemically determined and environmentally conditioned hetero- and homosexual instincts. This conflict brought on the psychosis.

Diabetes mellitus associated with adrenal tumour and hirsuties in women was described by C. Achard and J. Thiers in 1921. A new case was reported by H. C. Shepardson and E. Shapiro, who analysed 17 other collected cases of this syndrome. In these the diabetes mellitus was associated with a beard and in some cases with other evidences of endocrine disorder, such as thyroid enlargement and irregularity of menstruation. It was suggested that the diabetes mellitus was due to the effect on the pancreas of the abnormal adrenal cortex, but, although alterations in function of the adrenal cortex profoundly affect the production of insulin by the pancreas, diabetes was not constant in the adreno-genital syndrome. Therefore it is possible that in the Achard-Thiers syndrome, the rudimentary diabetes is also present apart from the abnormality of the adrenals.

In connexion with the diagnosis of the adreno-genital (or adreno-cortical) syndrome, which has been so extensively investigated at the Mayo Clinic, W. Walters *et al.* pointed out that in some cases in women the clinical manifestations have been those of Cushing's (basophilism) syndrome in which the habitus is not masculine, as in adrenal virilism, but of the 'buffalo obesity' type. In these anomalous cases of the adreno-cortical syndrome the clitoris is not enlarged, and the patient bears only a superficial resemblance to the almost completely masculinized female with an adreno-cortical tumour; these cases are spoken of as 'masquerading as pituitary basophilism'. Attention was also directed to the masculinizing effect of ovarian arrhenoblastomas, but the latter cases rarely show diabetes mellitus, hypertension, osteoporosis, and other incidental symptoms in the adrenal virilism group. The main difficulty therefore is in the differential diagnosis of the adrenal virilism from Cushing's syndrome. In Cushing's syndrome the clinical picture is much more constant than in the adreno-genital syndrome. Laboratory tests are not of much help in the diagnosis. Contrary to what might be anticipated from recent knowledge of Addison's disease there is not any definite change in the electrolytic pattern of the blood of patients with adrenal tumour or hyperplasia. In cases of primary carcinoma of the adrenal cortex, R. T. Frank found a high content of oestrogenic substance in the urine, only equalled by that in pregnancy, but, in 15 patients with symptoms of the adreno-cortical syndrome or of pituitary basophilism, the test was negative. The injection of air around the adrenals in order radiologically to demonstrate a tumour was carried out in a few instances, but it was found that it gave rise to considerable discomfort.

W. Walters and E. J. Kepler, in a paper covering the above ground also referred to the high mortality, approximately half, in 40 collected cases of adrenalectomy. This was often due to acute adrenal insufficiency, as the adrenal cortical tumour was so actively secreting the cortical hormone, the other adrenal presumably had ceased to secrete, and the lapse of some time would be necessary before it could resume functional activity. Treatment by cortical hormone should be commenced directly any suggestion of adrenal insufficiency appears after operation. With improvement in technique, and post-operative hormone treatment, the last 7 cases of adrenalectomy were successful.

Pseudo-sexual precocity.—W. A. Reilly *et al.* reported a case of pseudo-sexual precocity in a girl who had grown $5\frac{3}{4}$ inches from the fourteenth to the twenty-second month of her age. She had a deep voice and the mental aspect of a boy. The clitoris had first been noticed to be large at the age of 22 months, and pubic hair was also present and had been growing for 2 months. The clitoris protruded an inch from between the labia and was the size of a boy's penis of the same age. The blood pressure varied from 102/40 to 115/65 mm Hg, which is very high for that age. The bone age was less than 4 years, and X-ray examination of the left kidney region showed a mass, 6 inches in diameter, above the kidney. An irregular brown adrenal tumour was removed at laparotomy. The patient made a good recovery and post-operative irradiation was applied to the abdomen and lungs. Two years after operation the pubic hair had completely dropped out, the clitoris was smaller, and there was marked retardation of the rapid rate of growth. The general health was good and there were no metastases. Microscopical examination of the tumour showed it to be a cortical carcinoma.

A somewhat similar case to the above was reported by J. S. Richardson and W. R. S. Doll. This child, a female, was normal during infancy, but rapid growth took place between 2 and 4 years. The clitoris was noticed to be large at 18 months and grew disproportionately until the age of 4. Pubic hair was noticed at 18 months and grew very thick. The voice became gruff at 3 years, acne appeared at 4, and axillary and facial hair at 5. There was no vaginal haemorrhage, and the mother

had noticed that the vagina was very small during infancy. The girl appeared mentally normal.

Hyperfunction of the Adrenal Medulla

W. Bensis and A. Codounis of Athens, who recognized 3 forms of paroxysmal arterial hypertension, namely, (i) that engrafted on permanent hypertension, (ii) associated with a definite clinical syndrome, and (iii) associated with a chromaffin tumour of the adrenal medulla, a hypertensive *surrénalome*, or preferably called a *médullosurrénalome*, devoted special attention to the last form. A baker, aged 40 years, who had had gonococcal orchitis and genital atrophy, renal calculi, and pyuria, began to have attacks of paroxysmal hypertension 3 times a day, increasing to 10, 30, and reaching even 40 in the 24 hours; during the attacks the blood pressure rose from 140 to about 280 mm. Hg, and the pulse-rate from about 90 to about 120. The fundi showed neuro-retinitis and haemorrhages. Injections of adrenaline and also of atropine brought on attacks of paroxysmal hypertension, whereas eserine had an antagonizing action. Stress is laid on the presence during the attacks of hyperglycaemia without glycosuria. Cardiac failure came on and death occurred after a very severe attack of paroxysmal hypertension. The necropsy showed a chromaffin-celled tumour (phaeochromocytoma) the size of a tangerine orange in the medulla of the left adrenal; the right adrenal was normal in size and showed cortical adenomas. The heart was dilated and moderately hypertrophied, and the kidney showed compensatory hypertrophy and nephritis. The authors accept 15 reported cases of paroxysmal arterial hypertension due to an adrenal chromaffinoma.

Achard, C., and Thiers, J. (1921) *Bull. Acad. Méd. Paris*, **86**, 51.

Allen, C., Broster, L. R., Vines, H. W. C., Patterson, J., Greenwood, A. W., Marrian, G. F., and Butter, G. C. (1939) *Brit. med. J.*, **1**, 1220.

Bensis, W., and Codounis, A. (1939) *Bull. Acad. Méd. Paris*, **121**, 237.

Reilly, W. A., Lissner, H., and Hinman, F. (1939) *Endocrinology*, **24**, 91.

Richardson, J. S., and Doll, W. R. S. (1939) *Brit. med. J.*, **1**, 501.

Shepardson, H. C., and Shapiro, E. (1939) *Endocrinology*, **24**, 237.

Walters, W., and Kepler, E. J. (1938) *J. Amer. med. Ass.*, **111**, 1061.

— — — and Piper, M. G. (1938) *Proc. Mayo Clin.*, **13**, 353.

AGRANULOCYTOSIS

See also Vol. I, p. 261; Cumulative Supplement, Key No. 32; and p. 177 of this volume.

Aetiology

Amidopyrine, which is regarded as responsible for agranulocytosis by producing a state of the bone marrow comparable to the hepatic necrosis caused by cinchophen, was injected into the bone marrow and given by the mouth to 44 rabbits by A. B. Hansen, but did not cause agranulocytosis.

H. A. Shecket and A. E. Price, after reviewing the 9 recorded cases of fatal granulocytopenia due to sulphanilamide, recorded another case. In these 10 cases, the doses of sulphanilamide preparations ranged from 35 to 64 g. with an average of 50 g. The length of time of administration ranged from 15 to 30 days, the average being 27 days. The therapeutic benefit of sulphanilamide in a given condition should appear after 4 to 7 days, and, if no improvement is then noted, continuation of the drug is of doubtful value. The 10 cases showed toxic symptoms while sulphanilamide was being taken. Certain of these reactions should be considered as warning signals—cutaneous eruptions, hyperpyrexia, jaundice, gradual fall in red-blood cells and haemoglobin, and an abrupt rise or fall in white blood-cells. If symptoms persist or recur after decrease, or on resumption, of the drug, it should be permanently discontinued. Granulocytopenia was not manifest in 6 of the reported cases until one to 4 days after the drug was discontinued. Sulphanilamide should not be tried in the treatment of diseases in which its value is not established, unless the patients are under institutional supervision. Legislation is necessary to prevent dispensing the drug without prescription.

I. Abicht and J. Wienbeck reported a case of agranulocytosis in the puerperium

which was thought to be due to hormonal activity. The patient died nine months after discharge from hospital and the subsequent necropsy was described in detail by the authors. The absence of granulopoietic cells in the film of the sternal puncture, and the normal appearance of the megakaryocytes and the cells of the erythropoietic system, confirmed the diagnosis as a case of essential agranulocytosis. Sternal puncture showed no change from the first sternal puncture taken at the time of the disease. The authors drew attention to the remission in the state of the patient, who was discharged apparently cured, and who had the second fatal attack of agranulocytosis nine months later. The second attack started as a violent tonsillitis.

Abicht, I., and Wienbeck, J. (1939) *Med. Klinik*, **35**, 714.

Hansen, A. B. (1939) *Acta med. scand.*, **98**, 307.

Sheckel, H. A., and Price, A. E. (1939) *J. Amer. med. Ass.*, **112**, 823.

Treatment

Pentnucleotide.—M. C. G. Israels and J. F. Wilkinson report 4 cases of agranulocytosis and one of chronic neutropenia. Amidopyrine was the aetiological factor in 2 cases, one of which was fatal. No aetiological agent was discovered in the other cases. Three cases were fatal. Pentnucleotide was given to the 5 patients, in the non-fatal amidopyrine case it did not appear to increase the rate of recovery of the granular leucocytes, and in the fatal case no response was evoked. One case responded well to the treatment. The case of chronic neutropenia showed a transient increase in the granular leucocytes, but the clinical condition was unaffected. Ulceration of the oesophagus occurred in one case.

Israels, M. C. G., and Wilkinson, J. F. (1937) *Quart. J. Med.*, N.S., **6**, 35.

ALBUMINURIA

See also Vol. I, p. 273.

Aetiology

H. D. Niles investigated a series of 216 cases of scabies to discover whether any relationship existed between this condition and albuminuria. In this group only 16 showed the slightest trace of albumin at one examination. The tests (boiling and acetic acid) were performed prior to the patients receiving any treatment at the clinic, in order to eliminate the possible effect of therapy. Only 7 of the 16 patients could be followed up, and 4 of these failed to show albumin after disappearance of the scabies, while in 3 albuminuria persisted for many months after the eruption had disappeared. It was felt that in these 3 some underlying factor distinct from the scabies might be responsible for the continued albuminuria, and the author considered that the incidence of albuminuria found in this group (7.4 per cent) was no higher than that which might be found in routine urine analysis of normal subjects.

Niles, H. D. (1938) *Arch. Derm. Syph.*, N. Y., **38**, 19.

ALCOHOLISM

See also Vol. I, p. 280, and Cumulative Supplement, Key No. 36.

Toxic Effects

Acute Alcoholism

Alcohol tolerance.—A study of alcohol tolerance tests in normal and diabetic persons, and of the effect of pituitary extract, insulin, food, and forced water-intake on these tests is reported by H. Blotner. A dose of 0.6 c.cm. of absolute alcohol per kg. of body weight was administered. The solution generally contained 50 c.cm. of absolute alcohol, 50 c.cm. of grape-juice, and 150 c.cm. of water. The alcohol concentrations in blood and urine were examined in each case before the test meal and at half-hourly intervals for 4 hours afterwards, and were very slightly higher in patients with diabetes insipidus than in normal persons. While pituitary extract reduced these levels in both groups, yet the symptoms of alcoholic intoxication were increased in the former, perhaps due to the retention of more

alcohol in the tissues. In diabetes mellitus the blood and urine alcohol levels were appreciably higher than normal after ingestion of the alcohol, but the symptoms of alcoholic intoxication were about the same. The administration of insulin had no effect on the alcohol curves or on the symptoms of alcoholic intoxication. Ingestion of food before administration of the alcohol caused a definite decrease in the level of alcohol in both the blood and urine. Diuresis instituted by forced water-drinking did not dilute the concentration of alcohol in the urine, but increased the total amount of it excreted therein to approximately 1 to 3 per cent.

Relation to accidents.—R. L. Holcomb considered the causal relations of alcohol to accidents. The highest percentage of drinking drivers occurred in the early morning hours and at the week-end. The peak age for drinking drivers was 25 to 30. Investigation of many cases showed that, as the blood alcohol content increased, the number of drivers appearing in the personal injury accident group increased out of all proportion to that in the general driving population. As the amount of alcohol consumed increased accidents also increased, and at a rate somewhat proportionate to the increase in alcohol. Equal percentages of drinking drivers were found in the accident group and in the general population group at a point near 0.5 part of alcohol per 1,000 parts of blood, indicating that alcohol in that amount is not necessarily a significant cause of accidents. It had not been proved how important a cause-factor alcohol is, but the data gathered confirm a self-evident fact that alcohol is a major cause of automobile accidents.

Alcoholic amaurosis —F. D. Carrole and R. Goodhart reported 4 cases of acute temporary alcoholic blindness. In all cases there were total blindness, normal pupillary reactions to light and convergence, and normal fundi. The blindness improved within a few hours. All the patients had been drinking ethyl alcohol and all had been the subjects of head injury in the past. The diminished tolerance to alcohol following head injury is well known. The authors consider that a background of addiction to alcohol which was present in these 4 cases is probably necessary for the production of this type of amaurosis. They think that methyl alcohol poisoning in addicts is rare, and that amaurosis due to methyl alcohol poisoning is still rarer.

Treatment with coramine —G. Nideggen treated 30 cases of alcoholic intoxication with intramuscular injections of coramine after noticing the astonishingly rapid and satisfactory effect of the intravenous injection of 20 c.cm. of coramine in a very severe case of alcoholic coma. In milder cases 1 or 2 ampoules of 17 c.cm., and in more marked cases a large ampoule of 55 c.cm., were injected intramuscularly, and it was observed that the patient became sober within 10 to 25 minutes. The author concluded that this was the method of choice, with the added advantage that the intramuscular injection can be given by the nursing staff in the busy casualty departments. It helps diagnosis considerably by enabling the patient to answer questions soon after arrival in hospital, so excluding coma due to other causes.

Treatment of delirium tremens.—On the assumption that an increase in the pressure of the cerebrospinal fluid and cerebral oedema play a large part in the pathogenesis of delirium tremens, many workers have treated the condition by lumbar puncture and the intravenous administration of hypertonic solution. J. M. Thomas, E. V. Semrad, and R. M. Schwab noted that many delirium tremens patients are toxic and dehydrated on admission. They treated 40 such patients by lumbar puncture and hypertonic fluids, both intravenously and by mouth. A second group of 20 patients had no lumbar puncture and their intake of fluids was not restricted. None of the control patients received any alcohol while in hospital, and patients who were likely to have a raised cerebrospinal fluid pressure from any other cause were investigated. All cerebrospinal fluid readings obtained in these cases were normal. The results were equally good in both groups and Thomas, Semrad, and Schwab concluded that lumbar puncture has no effect in the treatment of delirium tremens.

The treatment of delirium tremens has been greatly improved. Piker found that 205 of 275 patients with delirium tremens developed the condition while they were still drinking, thus refuting the theory that the onset of the condition may be attributable to the sudden cessation of drinking. The theory that the patient should be dehydrated because he may have cerebral oedema has also been discarded. Nicholson and Taylor have shown that alcohol causes diuresis with retention of potassium which rapidly dehydrates the body, and may cause most of the symptoms of the alcoholic 'hangover'. Thomas, Semrad, and Schwab have demonstrated that patients with delirium tremens improve more rapidly if the intake of fluid is drastically increased. A litre of physiological solution of sodium chloride should be given

parenterally in addition to a minimum of 3,000 c.cm. by mouth daily. All vitamins should be given in large amounts, especially vitamin B₁. Paraldehyde is the best sedative. This regimen shortens the delirium and may save lives. Lumbar puncture is not indicated therapeutically but may be of use to show any evidence of injury to the brain.

Chronic Alcoholism

Hepatic cirrhosis.—E. M. Hall and W. A. Morgan described in 68 cases a special form of hepatic cirrhosis due to alcoholism, a progressive or active type which might conveniently be designated as subacute or progressive alcoholic cirrhosis. The liver, was large, 2,000 to 5,000 g., the average weight being 2,760 g., with a smooth or granular surface and fatty change. At least 80 per cent of these patients were chronic alcoholics, only one denying that he took alcohol. The Wassermann reaction was positive in 12, or 17.6 per cent of the 68 cases. A correct diagnosis was made in 36 cases, a partially correct diagnosis in 12 cases, and in 20 cases the diagnosis was wrong. Ascites occurred in 41, or 60 per cent of the cases, and jaundice in 34, or 50 per cent. The incidence of jaundice was much higher than that, 30 per cent, in 217 cases of all kinds of hepatic cirrhosis including chronic cases, from the same hospital (Los Angeles County), published by N. Evans and A. Gray, whereas the percentage of ascites was the same (60) in both series. The alcoholic responsibility for cirrhosis was shown by the increased incidence since 1932, when national prohibition was repealed. It was also pointed out that chronic alcoholics suffered from a low intake of carbohydrates, diminished storage of glycogen in the liver, and vitamin deficiency, and that the liver was thereby specially vulnerable to the toxic effects of alcohol.

Sclerosis corticalis laminaris alcoholica.—Four men aged 37, 51, 52, and 58 years, addicted to alcohol for many years, were examined by F. Morel. They had suffered from delirium tremens for some time, and some mental defect persisted until death. No sign of syphilis was observed and the cerebrospinal fluid was normal. At necropsy and on microscopical examination no sign of general paralysis or senile dementia was observed. In the third layer of the cortex proliferation of neuroglia was demonstrated. Symmetrical parts of the cortex were affected to the same degree. The frontal lobe was affected most severely. Both macroglia and microglia were increased. The number of nerve-cells in the third layer was diminished, but no characteristic alteration in these cells was observed. The myelinated supraradial fibres, outside the third layer, were diminished. No sign of Wernicke's polioencephalitis superior was observed in these 4 cases.

Effect on kidneys.—M. Bruger *et al.* investigated the effect of alcohol on the normal kidney and on the kidney of Bright's disease. Of the 21 cases studied 5 were free from renal disease, 5 had glomerulo-nephritis, 7 had chronic diffuse glomerulo-nephritis, and 5 had arteriosclerotic nephritis. They found that the ingestion of alcohol did not impair the function of the normal kidney. It also had no effect on the renal function of those suffering from acute and chronic diffuse glomerulo-nephritis, nor did it retard the recovery of such acute cases in this group as were improving. Alcohol produced a transient increase in the Addis count of patients with arteriosclerotic nephritis and temporarily increased the impairment of renal function. It often produced diuresis even in patients with impaired renal function. The amount of alcohol given was 50 to 200 c.cm. of a 25 per cent solution of ethyl alcohol or an amount of whisky equivalent to it.

Korsakow Syndrome

M. Rosenbaum and H. H. Merritt studied 50 typical cases of Korsakow's syndrome. The mortality-rate was higher in women (56 per cent) than in men (38 per cent). There was a progressive rise in the mortality-rate with every decade of life. The authors considered that a rapid onset was an unfavourable factor. Of the patients who became quiet and co-operative within a week of admission, only 23 per cent died. The severity of the polyneuritis had no significant relation to the mortality rate, whereas a high leucocyte count or low red-cell count was a bad sign. Eleven out of 22 patients who received no special therapy died, but no death was recorded among 7 who received vitamin B₁ intravenously in addition to a full diet of high caloric value and rich in vitamins.

Wernicke described a disease affecting the nuclei of the nerves to the eye muscles and causing paralysis of the muscles, a reeling gait, and disturbances of consciousness, as encephalitis haemorrhagica superior. The syndrome may be associated with Korsakow's psychosis. A. D. Ecker and H. W. Woltman reported a case of Wer-

nicke's disease in a 20 year old woman following sulphuric acid poisoning. Necropsy showed punctate haemorrhages in the third ventricle, the corpora quadrigemina, and the retina. The authors also reported a case of their own associated with chronic atrophy of the liver and the gastro-intestinal mucous membrane. They suggested that the central nervous system condition was due to a deficiency caused by poor absorption. Retinal haemorrhages occur in vitamin B deficiency, and the lesions of Wernicke's disease are said to have been produced in animals receiving a diet deficient in vitamins. Sometimes the ingestion of vitamins B and C in large doses has cured the condition.

- Blotner, H. (1939) *New Engl. J. Med.*, **220**, 283.
 Bruger, M., Localio, S. A., and Guthrie, N. W. (1939) *J. Amer. med. Ass.*, **112**, 1782.
 Carrole, F. D., and Goodhart, R. (1938) *Arch. Ophthalm., N.Y.*, **20**, 797.
 Ecker, A. D., and Woltman, H. W. (1939) *J. Amer. med. Ass.*, **112**, 1794.
 Evans, N., and Gray, A. (1938) *J. Amer. med. Ass.*, **110**, 1159.
 Hall, E. M., and Morgan, W. A. (1939) *Arch. Path.*, **27**, 672.
 Holcomb, R. L. (1938) *J. Amer. med. Ass.*, **111**, 1076.
 Morel, F. (1939) *Rev. neurol.*, **71**, 280.
 Nicholson, W. M., and Taylor, H. W. (1938) *J. clin. Invest.*, **17**, 279.
 Niedeggen, G. (1939) *Munch. med. Wschr.*, **86**, 893.
 Piker, P. (1937) *Amer. J. Psychiat.*, **93**, 1387.
 Rosenbaum, M., and Merritt, H. H. (1939) *Arch. Neurol. Psychiat., Chicago*, **41**, 978.
 Thomas, J. M., Semrad, E. V., and Schwab, R. M. (1938) *Amer. J. med. Sci.*, **195**, 820.
 — — — (1939) *Ann. intern. Med.*, **12**, 2006.

Treatment of the Alcoholic

Benzedrine.—W. Bloomberg discussed the efficacy of benzedrine sulphate in the treatment of chronic alcoholism and gave reports of 21 cases. He was led to try this treatment by the observation that benzedrine was effective in relieving the 'hangover' on the morning after excessive drinking, and that, when taken before drinking, it appeared to increase the capacity of the chronic alcoholic to consume alcohol without intoxication. Patients were first given two 10 mg. tablets of benzedrine sulphate daily; this dose was increased by a further 10 mg. in the late afternoon in some cases and decreased in one case. Each patient was seen at weekly intervals for several weeks, then at fortnightly and finally at monthly intervals. There was no evidence of habit formation, nor any disturbing effect, and the patients stated they felt alert and energetic and no longer felt the need to drink. The appetite and the blood pressure were unaffected, and no weight was lost. In all except 4 cases, a period of abstinence occurred significantly longer than any in the year or two preceding treatment; these periods of abstinence varied from 2 weeks to 13 months, and in 6 cases were longer than 4 months. In 6 patients the drinking habits were so modified that, even though they had a few relapses from total abstinence, they were able to resume their place in the family, or in business. It was felt that this interval of sobriety would permit of the institution of psycho-therapeutic methods.

Cardiac Complications

H. Gounelle and S. Follin observed a case of alcoholic cardiac decompensation in a soldier aged 26 suffering from an insufficiency of his right heart; wide-spread oedema, ascites, painful hepatomegaly, gallop rhythm, and a systolic murmur over the right ventricle were the main clinical signs and the patient had a tachycardia of 120. Digitalis and strophanthin were of no avail, and the patient lost weight, until the resemblance of his cardiac condition to that of the beri-beri heart was recognized. Treatment with vitamin B₁ yielded an astonishingly quick result, as in about 5 days the patient's condition returned to normal. The authors quote the similar good results obtained by others with this treatment in alcoholic insufficiencies of the heart.

- Bloomberg, W. (1939) *New Engl. J. Med.*, **220**, 129.
 Gounelle, H., and Follin, S. (1939) *Bull. Soc. méd. Hôp. Paris*, **55**, 879.

ALKALOSIS

See also Vol. I, p. 292.

Biochemical Test

L. C. Gatewood used nickel sulphate to determine the quantity of carbonate excreted in the urine. A few c.cm. of a 20 per cent nickel sulphate solution is poured into a test tube, and filtered urine is allowed to run gently down the side of the test tube, the presence of soluble carbonate being revealed by the formation of a white ring of precipitate at the junction of the two fluids. The thickness of the ring affords a method of calculation of the amount of carbonate present in various samples of urine. The quantity of carbonate present in the urine of normal subjects receiving a general diet is insufficient to produce a positive result. The ingestion of 4 g. of sodium bicarbonate produced positive results within an hour in those patients receiving alkaline treatment for peptic ulcer. When alkalosis developed there was a prompt decrease in the excretion of carbonate to the point where a positive reaction could no longer be demonstrated. With a return to normal acid-base equilibrium there is also a return of normal carbonate excretion.

Gatewood, L. C. (1938) *Amer. J. digest. Dis.*, **5**, 461.

ALLERGY

See also Vol. I, p. 302, and Cumulative Supplement, Key Nos. 40-52

Aetiology

E. D. Osborne and H. L. Walker have carried out painstaking investigations of contact and environmental allergy in eczema of infants and children. There is no evidence of congenital specific epidermal sensitivity, but a 'susceptibility to sensitization' is inherited. The authors have found routine scratch, intradermal, and patch tests of little value, and consider that actual clinical trials are more important. A highly developed detective sense and infinite attention to details of history are essential in determining the cause of eczema in infants. Confinement to hospital with removal of all possible offending substances from the child's vicinity, clothing, and diet, was the most satisfactory method of treatment. By this means 50 per cent were cured in 4 to 8 weeks, and a further 35 per cent improved. Three case reports are given. It is believed that trans-epidermal absorption of water-soluble protein allergens through both inflamed and non-inflamed skin explains many of the clinical facts observed in patients sensitized to these allergens.

Biochemistry

Anaphylaxis is thought to be caused by histamine or a histamine-like substance. If this assumption be correct it should be possible to desensitize a sensitized animal by rendering it refractory to histamine. L. Farmer gave intra-abdominal injections of increasing doses of histamine to fully sensitized guinea-pigs for 12 to 18 days, 13 to 15 days after the sensitizing injection of serum, when the animals are usually highly sensitized. Young virgin guinea-pigs were used. The concentration of horse-serum, the specific antigen needed to bring about contraction of a strip of uterine muscle suspended in it, was then noted and it was found that a greater concentration was needed than in animals who had not been desensitized with histamine, i.e. the muscle was more refractory. Using normal unsensitized guinea-pigs it was found that their uterine strips were less sensitive to histamine than those of animals which had already received injection of histamine. Farmer concluded from these experiments that histamine is responsible for the anaphylactic contraction of plain muscle.

H. A. Rusk *et al.* studied the serum potassium content of normal persons and of patients with allergic conditions. In a group of 20 acute and chronic urticarias it was definitely raised above normal. This rise was most marked during an attack, the figure decreasing to lower levels as the skin condition subsided, but in any case the levels remained higher than normal. The serum potassium content was also found to be raised in asthmatic patients. The average level for a normal person was 19.5 mg. per 100 c.cm. of serum; in urticaria the average was 23.4 mg., and in acute bronchial asthma 24.4 mg. It was argued that an increased potassium content of the serum indicated that the cells were depleted of their normal content.

Hence, potassium salts were administered with insulin and dextrose. These two substances drove potassium back to the cells and established the electrolyte equilibrium. Insulin and dextrose, in combination or separately, were effective in lowering the serum potassium levels. The quantitative relationship between the size of dose of insulin and the subsequent lowering of potassium levels was entirely different during acute and symptom-free periods. In one patient a drop from 22 mg. to 16.6 mg. was found during an asymptomatic period, and, with the same dosage of insulin during an acute attack, the drop was from 24.5 mg. to 23.7 mg.

Actiological Factors

H. J. Parkhurst and J. A. Lukens report a case of severe dermatitis of the eyelids following the instillation into the eye for local anaesthesia of a 2 per cent solution of butyn. This is only the fourth case of its kind reported in medical literature. Butyn in a 2 per cent solution is used as a surface anaesthetic, in a 5 to 10 per cent solution as an anaesthetic throat-spray, and in a 2 per cent concentration as an ophthalmic ointment. The severe dermatitis was accompanied by intense itching, and later by vesiculation and oedema; the eye was swollen shut. An erythematous vesicular streak, about 5 mm. wide, extended down the cheek to the chin, apparently following the path along which the solution of butyn had run. The patient was advised to wash the area night and morning with soap and water, and to apply moist compresses of saturated boric acid solution constantly during the day, and at night a little plain zinc oxide ointment. The dermatitis subsided in a week. Patch tests with the solution of butyn and with the zinc sulphate solution were applied to the patient's arm, and removed 24 hours later. The reaction to the butyn was positive, and increased in intensity. In 3 days the patch was red, vesicular, and oedematous, and the arm swollen and painful.

W. Gronemeyer reported a case of allergy to menthol, a condition hitherto unrecognized. The patient had giant urticaria, and an intense pruritus found to be due to suppositories containing menthol. The antigenic character of menthol was subsequently tested by smearing 1 per cent, 2 per cent, and 5 per cent menthol-glycerin ointment on the skin of the patient, and covering it with a dry dressing; a positive reaction, namely, erythema and pruritus, was obtained.

The growing popularity of the West Indies as a resort for tourists and the retired is leading to an increasing number of cases of manchineel poisoning. K. Vigors Earle described the tree and its poisonous effects and their treatment. The tree grows in South America, Central America, and the West Indies along the sea shore, just above high-water mark, and is rarely found inland. Of this tree there are 2 types, the leaves of one resembling the holly and of the other the camellia. The male flowers are yellowish and the female greenish. The fruit resembles the crab-apple and may be green, greyish brown with longitudinal grooves, or the colour and size of a russet apple. The lactiferous vessels, present throughout the tree, on section discharge white liquid latex which thickens and darkens on exposure to air. In man, contact with the tree may cause erythema and blistering of the epidermis. Intense conjunctivitis may be set up by direct contact by the fingers, or by water falling from the trees. The fruit is fragrant and appetizing and its ingestion or chewing causes severe blistering and swelling of the lips and buccal mucosa with excessive salivation. If much of the juice is swallowed a severe gastro-enteritis, with blood-stained diarrhoea and shock, results which in some cases have been followed by coma and death. Inhalation of sawdust from the wood of the tree causes rhinitis and cough, and sometimes nasopharyngitis, laryngitis, or bronchitis. The lethal dose is between 30 and 35 g. of the fruit. Post-mortem findings in man have not been recorded but in animals inflammation and desquamation of the buccal and gastro-intestinal tracts occur.

It has been suggested that the reaction to the manchineel and its fruits may be an allergic one. The respiratory changes produced by inhalation of the sawdust support this view. It is recommended that the juice on the skin should be washed off with sea-water as a prophylactic measure. Blisters on the skin should be kept aseptic and, if extensive, treated like burns of the second degree. Buccal lesions may require local anaesthesia, and application of glycerin of borax and alkaline mouth-washes is indicated. If the fruit is swallowed, vomiting must be induced and the gastritis treated with rice-water and almond oil. Rectal feeding may be necessary if the mouth is severely blistered. Shock must receive adequate treatment.

Earle, K. V. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 363.

Farmer, L. (1939) *J. Immunol.*, **36**, 37.

- Gronemeyer, W. (1939) *Dtsch. med. Wschr.*, **65**, 756.
 Osborne, E. D., and Walker, H. L. (1938) *Arch. Derm. Syph.*, N.Y., **38**, 511.
 Parkhurst, H. J., and Lukens, J. A. (1939) *J. Amer. med. Ass.*, **112**, 837.
 Rusk, H. A., Weichselbaum, T. E., and Somogyi, M. (1939) *J. Amer. med. Ass.*, **112**, 2395.

Asthma

Treatment

In discussing the use of drugs in allergic conditions, H. Gold stated that the underlying disturbances responsible for the symptoms should be considered. In the case of asthma several abnormal factors were encountered, the result of most of them being the impairment of the movement of air through the pulmonary tree, and interference with the diffusion of gases. Drugs such as ephedrine and adrenaline used in the treatment of asthma acted by stimulating the sympathetic, thus causing relaxation of the bronchial musculature and constriction of the blood vessels; blocking of the parasympathetic may be produced by the use of atropine or belladonna, with resulting reduction in secretion and relaxation of the bronchial muscle. Relaxation of smooth muscle could be obtained by theophylline or caffeine, and capillary permeability reduced by calcium salts. Theophylline was particularly effective in those patients who had developed an adrenaline fastness. It was mentioned that adrenaline given intravenously produced the most dramatic effect in asthma. Although the effect of ephedrine was less intense and striking, it had the advantage of being potent when given by mouth. To secure the best effect it should be given with phenobarbitone or a similar sedative. This helps to eliminate the nervous effect and tachycardia.

The use of iodides was recommended in cases in which it became necessary to render the mucus more liquid and easier to expectorate. Morphine should be used with extreme caution, but its property of stimulating the parasympathetic system made it of value in some cases.

Ragweed pollen.—In the immunization of conditions such as asthma many attempts have been made to substitute oral administration for hypodermic injection with its attendant expense and discomfort. T. B. Bernstein and S. M. Feinberg tried oral doses of pollen extracts in 20 asthmatic patients allergic to ragweed. One drop of a 1 in 33 extract of ragweed pollen was given as an initial dose, rising to 10 to 30 drops 3 times a day. These small doses, considered as probably inadequate, were necessary because larger doses caused gastro-intestinal symptoms. Of the 20 patients, 18 did not receive any benefit from the treatment, and the other 2 obtained some moderate relief only.

On the other hand H. J. Black found that, though in some patients the oral administration of ragweed pollen produced satisfactory results, the percentage of patients so relieved was lower than that obtained by hypodermic treatment. An initial dose of 500 units once daily was administered to 40 patients within a week of the onset of the ragweed season. This was increased by 500 units each day until the symptoms subsided or a dose of 4,000 units was reached. With the larger doses 1,000 units were taken at a time. The pollen was taken fasting. The interesting observation was made that, in cases receiving hypodermic treatment who showed a violent reaction, the oral administration of pollen immediately lessened that reaction so that the hypodermic injection could be pushed to the desired limit.

Bernstein, T. B., and Feinberg, S. M. (1938) *Arch. intern. Med.*, **62**, 297.

Black, H. J. (1939) *J. Allergy*, **10**, 156.

Gold, H. (1939) *J. Amer. med. Ass.*, **112**, 1335.

Urticaria

Treatment

Autohaemotherapy.—A method of desensitization against eruptions occurring at the same time as menstruation is proposed by J. Geber who considered that an antigen was present in the blood for a short period, possibly only for hours, when the eruption was at its height and the symptoms culminated. Forty to 50 c.cm. of blood were taken from a patient and the serum put into a rubber-capped bottle, 0.3 per cent phenol being added to ensure sterility. Injections of 0.4 c.cm. of serum were made

daily or every second day into two areas in corresponding positions at some distance from each other. A mild reaction was observed at the site of injections, and variations in menstruation were sometimes found to occur subsequently. Desensitization was usually established after the second period, treatment being given intermenstrually, and remaining adequate in some patients for years. Cases of bronchial asthma and trigeminal neuralgia also responded to this treatment.

Insulin shock.—W. Bruhl gave an insulin injection to a patient suffering from urticaria for diagnostic purposes, and found that the skin eruptions disappeared. He tried insulin in 8 more cases of urticaria, in 4 cases of angioneurotic oedema, and in 17 cases of allergic eczema. In one case of circumscribed vasoneurotic eczema of the eyelids with complete closure of the eyes, one injection of insulin was sufficient to allow opening of the eyes after 4 hours. The results were similarly quick and good in all the other cases mentioned above. Most patients had no more recurrences, even when they had had recurrences of the allergic skin conditions for years. The main effect of the insulin injection from a physiological point of view is an increase in the blood of adrenaline, the therapeutic effect of which in allergic conditions is well known. Insulin has no effect upon the allergy: it is the reactive increase of adrenaline which is effective. If insulin was given together with a corresponding amount of glucose to prevent hypoglycaemia, no effect was observed. The dose used was 10 units of insulin, injected intravenously. The author thinks that there is a constant increase of adrenaline production after the injection.

Alkaline diet and sodium bicarbonate.—H. Luckner and E. Mann described a case of severe urticaria in which the closest examination revealed no cause for the condition other than repeated physical strain. Further investigations revealed that the carbon-dioxide saturation of the blood, together with the resulting disturbance of the acid-base balance, was the most important aetiological factor. The patient also complained of repeated attacks of migraine. Treatment with an alkaline diet and 3 g. of sodium bicarbonate daily resulted in a complete cure, but, on recurrence of the symptoms, this was supplemented by the daily administration of phenobarbitone: this reduced the irritability of the medulla, which was also a factor in this case.

Bruhl, W. (1939) *Dtsch. med. Wschr.*, **65**, 326.

Geber, J. (1939) *Brit. J. Derm.*, **51**, 265.

Luckner, H., and Mann, E. (1939) *Klin. Wschr.*, **18**, 767.

Serum Sickness

Treatment

Histaminase.—The hypothesis was put forward that serum sickness was caused by a release into the tissues of histamine following the combination of serum protein antigen and antibodies. Histaminase, a compound which contains the active principle of the histamine-inactivating substance found in tissues, was used in the prophylaxis and treatment of serum sickness. This preparation was used by L. Foshay and O. E. Hagebusch orally as enteric-coated tablets each containing 5 histamine detoxicating units and in ampoules for intramuscular injection, each representing one detoxicating unit. Of 8 cases, in each of which histaminase was administered orally, 6 were improved or totally relieved of symptoms of serum sickness within 10 to 36 hours. In 2 of these cases mild symptoms persisted for 2 or 4 days. A group of 12 patients received intramuscular injections and obtained improvement or marked relief in a period varying from 12 to 72 hours. A thirteenth patient was also reported to have made a good recovery.

The prophylactic use of histaminase in 8 patients resulted in absence of serum sickness in 6 cases. One of them continued to receive gas gangrene antitoxin, the total dose of which was 453,000 units. Two patients of this group had wheals but no other symptoms. Four cases received 60 c.cm. and one 90 c.cm. of unrefined antibrucella horse serum. Two received 30 c.cm. of unrefined antitularense horse serum. The intramuscular dosage was one ampoule night and morning for 5 injections, with initial increase in the dose in severe cases. In tablet form the optimal dose appeared to be 4 to 5 tablets 3 times a day before meals for the first day, followed by 3 or 4 tablets 3 times a day for the next day or two. No reactions or untoward effects were apparent as the result of this treatment.

Other measures.—F. Szirmai examined the effect of vitamin C on allergic individuals, and concluded that it had no effect in preventing serum sickness or in lessening the anaphylactic reaction. Using an inverted anaphylactic test in which the antigen is injected first and the antibody-containing serum afterwards, the author was able to

prove the uselessness of fractioning a serum dose and desensitizing allergic individuals in general. In 11,000 injections of serum, anaphylactic reactions never resulted in death, and the author contended that the use of calcium, strophanthin, or glucose for anaphylactic reactions is quite sufficient. Intravenous serum treatment should be given only in a hospital where the patient can be observed, and serum sickness be treated in its early stages.

Foshay, L., and Hagebusch, O. E. (1939) *J. Amer. med. Ass.*, **112**, 2398.

Szirmai, F. (1939) *Arch. Kinderheilk.*, **117**, 56.

ALZHEIMER'S DISEASE

See also Vol I, p. 354.

Aetiology and Morbid Anatomy

E. Grunthal and O. Wenger reported the case of a man of 60 years who lost his memory, became irritable, and whose speech became unintelligible; he became somewhat stiff, but he did not look like a case of typical Parkinson's disease. He died 2 years later from pneumonia. At necropsy marked atrophy of the myocardium and liver was seen. On microscopical examination signs of Alzheimer's disease were observed in his brain. The father as well as a sister of this patient had probably been affected by Alzheimer's disease. Another sister, still alive, also suffered from pre-senile dementia. The authors further reported the history of a woman of 83, affected by senile dementia for several years. At necropsy mild signs of arteriosclerosis were observed in her brain, there were no definite changes in the grey matter, but marked hydrocephalus was present. On microscopical examination senile plaques were not observed, but only the mild changes in the fibrils described by Alzheimer. This unusual finding may have resulted from the fact that the brain had not shrunk, but perhaps the fact that this patient had lived in a tropical climate for many years may have been of some importance.

Grunthal, E., and Wenger, O. (1939) *Msch. Psychiat. Neurol.*, **101**, 8

AMENORRHOEA

See also Vol I, p. 359

Treatment

Pregneninonol — B. Zondek and S. Rozin succeeded in initiating uterine haemorrhage in normally menstruating women during the intermenstrual stage by the intramuscular injection of progesterone 10 mg daily for 5 days, beginning shortly after menstruation. In secondary amenorrhoea, haemorrhage could be induced by the oral administration of pregnenolone without preliminary treatment by oestrogenic hormone. The effective dose of pregnenolone required orally (300 mg) was about 6 times greater than the effective dose of progesterone (50 mg) given by intramuscular injection.

Zondek, B., and Rozin, S. (1939) *Lancet*, **1**, 504.

AMPUTATION

See also Vol. I, p. 378.

Complications of Amputations and After-Care

Phantom-Limb Pain

W. K. Livingston treated 10 cases of phantom-limb pain following amputation of an upper extremity with injection of procaine hydrochloride near the thoracic sympathetic ganglia. Injection at the level of the third thoracic ganglion produced better results than injection at the level of the stellate ganglion. The pain was tearing, cutting, not referred to a particular spot in a single digit, and different from that due to a hypersensitive neuroma, and might occur in the absence of a neuroma.

The pain was probably due to a physical lesion but what this was exactly was unknown. Other symptoms referable to the phantom limb were cramp, and especially tension. The stump was sometimes cold, sometimes discoloured and oedematous, and often associated with excessive sweating on that side of the body. The pain was associated with insomnia, emotional instability, and increased sweating. The injection produced in 8 of the cases immediate relief, the phantom limb becoming warmer, and the feeling of tension lessening and gradually disappearing. Sometimes the relief produced by injections of procaine hydrochloride lasted for a very long period.

Livingston, W. K. (1938) *Arch. Surg., Chicago*, **37**, 353.

ANAEMIA

See also Vol. I, p. 408; Cumulative Supplement, Key No. 59; and p. 53 of this volume.

Pernicious Anaemia

Clinical Picture

Gastroscopy.—R. Schindler and A. M. Serby examined with the gastroscope the conditions of the stomach in pernicious anaemia in 23 patients, 9 of whom were examined before they had any treatment, and 14 after adequate treatment; 3 of the 23 patients were examined both before and after treatment. All the patients before examination showed superficial gastritis and/or atrophic gastritis, either patchy or diffuse. After adequate treatment, in 7 patients the mucosa of the gastric antrum was normal, whereas in 4 patients there was not any improvement. These results could only be explained as evidence that there were 2 distinct forms of gastritis, namely, (i) disordered function of the cells which secrete the anti-anaemic factor; and (ii) secondary degeneration of the superficial epithelium with genuine inflammation which was usually accompanied by the glossitis and intestinal change of the same character. In 3 of the 23 cases there was a typical, apparently not inflammatory, adenoma of the stomach, thus confirming the recognized occurrence of polypi in the stomach in pernicious anaemia.

Serum-bilirubin.—J. Mills and C. A. Mawson found that the bilirubin content of the serum of 85 patients with pernicious anaemia was considerably greater than that of an equal number of normal persons. Of the pernicious anaemia patients, 93 per cent had serum-bilirubin greater than 0.4 mg. per 100 c.cm., whereas 91 per cent of normal patients had less than 0.4 mg. per 100 c.cm. The mean serum-bilirubin was 0.98 ± 0.06 mg. per 100 c.cm. in pernicious anaemia patients and 0.31 ± 0.02 mg. per 100 c.cm. in normal persons. In 53 patients with pernicious anaemia controlled by liver therapy, the serum-bilirubin was 0.31 ± 0.03 mg. per 100 c.cm. Specific treatment is, therefore, shown to reduce the raised serum-bilirubin to normal levels.

Treatment

W. P. Murphy and I. Howard treated 176 clinic patients with intramuscular injections of liver extract for periods ranging from 6 months to 6 years. With the idea of maintaining the erythrocyte count continuously at 5,000,000 cells per c. mm.—a level which will ensure for the patient the best possible protection against the development of neural disturbances or the further progress of those already existing—133 received an injection of 3 c.cm. of liver extract (Lederle) at average intervals of 3.7 weeks. Of the total group 31 received an injection of 1 c.cm. of a more highly concentrated liver extract at average intervals of 3.6 weeks in order to maintain the erythrocyte count at the same level. Neither age nor sex definitely influenced the amount of anti-pernicious anaemia substance necessary for maintenance. The intramuscular injection of 1 c.cm. of liver extract containing 15 U.S.P. Anti-Anaemic Preparations Advisory Board units of anti-pernicious anaemia potency administered at intervals averaging approximately 3½ weeks was sufficient to maintain a normal state of the blood and to prevent or arrest neural damage.

Mills, J., and Mawson, C. A. (1938) *Lancet*, **2**, 1455.

Murphy, W. P., and Howard, I. (1939) *J. Amer. med. Ass.*, **112**, 106.

Schindler, R., and Serby, A. M. (1939) *Arch. intern. Med.*, **63**, 334.

Achrestic Anaemia

Treatment

Splenectomy.—In macrocytic haemolytic anaemia, S. C. Dyke and F. Young pointed out that splenectomy, by removing a quantity of reticulo-endothelial tissue actively engaged in red-cell phagocytosis, is slightly more beneficial than is usually admitted. It was not, however, curative and its action did not compare with its efficacy as a measure in other conditions such as acholuric jaundice.

Dyke, S. C., and Young, F. (1938) *Lancet*, **2**, 817.

Tropical Megalocytic Anaemia

Differential Diagnosis

L. E. Napier discussed fully the difference between tropical megalocytic anaemia and pernicious anaemia, specially emphasizing the absence of neurological symptoms in the former, which also exhibited glossitis much less frequently. In macrocytic anaemia the blood picture showed a less marked poikilocytosis, no increase in the reticulocytes and, in the pregnant and non-haemolytic varieties, no leucopenia. The indirect van den Bergh reaction, which is positive in pernicious anaemia, is always negative in macrocytic anaemia.

The reaction of the two diseases to treatment also showed marked contrasts. Yeast extract or marmite in average doses brought about a cure in macrocytic anaemia, but only in 10 out of 18 cases of pernicious anaemia. Anahaemin, so successful with the latter, even in maximal doses sometimes failed with the former, though campolon achieved equal success with both. It was not considered that the food substance which is deficient in tropical macrocytic anaemia and Castle's extrinsic factor in pernicious anaemia are identical, but that the deficiency in tropical macrocytic anaemia is that of an independent haematopoietic principle.

The relation between the haemolytic and non-haemolytic types of tropical macrocytic anaemia was discussed by the author, who pointed out that malaria is an important predisposing factor in the haemolytic type. Further clinical experimental investigations are suggested along the lines of careful quantitative work, only purified fractions of autolysed yeast and liver extract being used.

Treatment

The findings of L. E. Napier *et al* regarding the administration of anahaemin in tropical macrocytic anaemia are reported. Evidence of 3 groups was found, in the first of which the deficiency was the same as in pernicious anaemia. In this group anahaemin was curative. In the second group the marmite principle was deficient, and marmite or liver therapy was curative, while in the third group the deficiency was compensated by some principle peculiar to campolon, but other liver extracts were not effective. The administration of campolon furnished good results. Anahaemin was used in the treatment of 6 pregnant women, and in one case a good result was noted. In 2 there was a less marked response. The remaining 3 gave no information of any value. A second group of 8 Indian males was similarly treated, and in 2 cases the specific action of anahaemin was demonstrated.

L. Wills and B. D. F. Evans consider that tropical megalocytic anaemia does not respond to the more highly purified liver extracts which contain in relatively pure form the liver principle which is curative in pernicious anaemia, although crude liver extracts and autolysed yeast extracts are curative. This demonstrates the presence of a new haemopoietic factor in crude liver and autolysed yeast extracts which is effective in the treatment of the tropical diseases.

Napier, L. E. (1939) *Indian med. Gaz.*, **74**, 1.

— Das Gupta, C. R., Chaudhuri, R. N., Sen, G. N., Rai Chaudhuri, M. N., Sen Gupta, P. C., and Majumder, D. N. (1938) *ibid.*, **73**, 385.

Wills, L., and Evans, B. D. F. (1938) *Lancet*, **2**, 416.

Megalocytic Anaemias

Aetiology

W. H. Barker and L. E. Hummel reported 2 cases and analysed 49 others, regarded as examples of megalocytic anaemia associated with intestinal stricture or anastomosis. This was stated to be a definite disease, and not a coincidence of idio-

pathic pernicious anaemia and an intestinal lesion, and as intimately bound up with stagnation and putrefaction of the intestinal contents. Out of the 51 patients, the first reported in 1893, 36 were dead; 25 were examples of stricture of the small intestine, 7 of stricture of the colon, 13 of entero-enterostomy, 5 of fistulous communications between parts of the intestine, and one of diverticulosis. Analysis of the state of the bone marrow in 11 cases showed that it was very similar to, if not identical with, that in Addisonian anaemia and that in the anaemia of sprue. In 39 cases the anaemia was stated to be macrocytic, in 32 hyperchromic, and in 30 there was leucopenia. Achlorhydria was present in 19 and absent in 17 cases; glossitis was noted as present in 18 and absent in 10 cases. As regards treatment and its results, the cases were divided into 4 groups: (i) 23 patients did not receive any surgical or liver treatment; 22 of these were dead. (ii) 9 patients were operated upon, but did not have any liver treatment; 5 of these died so soon after the operation that its influence on the anaemia could not be estimated. (iii) 9 patients were given liver extract only, and (iv) 10 patients were operated upon, and given liver extract; 3 died soon after operation. Stress was laid on the essential importance of operative removal of intestinal stricture and fistulous communications, though in some instances treatment by liver extract might be helpful.

Barker, W. H., and Hummel, L. E. (1939) *Johns Hopk. Hosp. Bull.*, **64**, 215.

Hypochromic Anaemia of Pregnancy

Treatment

R. Gottlieb and G. J. Strean conducted a haematological study of 525 consecutive cases of pregnancy. Of these 275 cases received no therapy; of the remaining 250, 50 were treated with iron and ammonium citrate 30 grains 3 times daily; 50 were given 6 grains of ferrous carbonate and $\frac{1}{16}$ grain of copper 3 times a day; 50 were treated with 5 grains of reduced iron 3 times a day, and 100 with ferrous sulphate 15 grains combined with vitamin B from yeast concentrate. Normal haemoglobin figures were attained in all groups in from 4 to 6 weeks. It is stressed that maternal anaemia is associated with a greater foetal polycythaemia which is developed to overcome the normal degree of anaemia in which the foetus lives before birth. Large quantities of iron are utilized but apparently the iron storage of the foetus of an anaemic mother is deficient, thus resulting in anaemia in the early months of life. This may be prevented by iron therapy.

Gottlieb, R., and Strean, G. J. (1939) *Surg. Gynec. Obstet.*, **68**, 869.

Hypochromic Deficiency Anaemias of Infancy

Incidence and Aetiology

J. H. Hutchison investigated the incidence and aetiology of nutritional anaemia in 300 infants in a large industrial area in Glasgow and found that 26 per cent of the breast-fed, and 35 per cent of the bottle-fed, infants had haemoglobin values at least 10 per cent below Mackay's normal values for their ages. These percentages become much greater if infants under the age of 6 months are excluded. The main aetiological factors were a deficient antenatal storage of iron, deficient iron content of breast milk, an undue prolongation of an exclusively milk diet, low birth-weight, and infections. Because of the high mortality and morbidity rates associated with anaemia in infants Hutchison stressed the importance of prophylaxis, e.g., by administration of $\frac{1}{4}$ to 9 grains of iron and ammonium citrate daily from the age of 2 months. Dried milk to which iron has been added may be used, and the early inclusion of iron-containing foods in the diet, e.g., broth, vegetable purée, and yolk of egg, at 4 or 5 months of age is very beneficial.

Treatment

C. H. Smith carried out 105 periodic observations on the sedimentation rate and other haematological factors in 16 cases of nutritional anaemia in infants and children. He found that in many cases the sedimentation rate was not increased, and in some was actually slower than normal. In 11 cases uncomplicated by infection, in which normal or slightly accelerated rates were noted before treatment, retardation occurred with the administration of iron. In 5 children in whom infection was also present, elevation of the sedimentation rate persisted after iron therapy, in spite of the regeneration of haemoglobin and red blood-cells. Of these

16 children, 10 were treated with ferrous sulphate, 5 with iron and ammonium citrate, and one with a combination of the two. Smaller doses of ferrous than of ferric salts were necessary to slow the sedimentation rate. It is suggested that the sedimentation rate should be used as an additional indication as to the efficacy of iron therapy in anaemia.

F. Bodart and R. Klima quoted from Starkenstein that iron was absorbed only when in the ferrous form, 1 g. of ferrous chloride daily being a sufficient dose in anaemia. Ferrous compounds, however, were easily oxidized by the atmospheric oxygen into ineffective ferric compounds. The authors tried various complex ferrous compounds, especially green iron and ammonium citrate, which contains about 13 per cent of iron and is easily digested. A dose of 6 g. is necessary. Of other preparations, iron and ammonium tartrate, iron and potassium tartrate, and iron and sodium tartrate, were the most effective, given in doses of approximately 4 g.

Bodart, F., and Klima, R. (1939) *Med. Welt*, **13**, 342.

Hutchison, J. H. (1938) *Arch. Dis. Child.*, **13**, 355.

Smith, C. H. (1938) *Amer. J. Dis. Child.*, **56**, 510.

Starkenstein (1930) *Brugsch, T. Spezielle Pathologie und Therapie innerer Krankheiten*, Berlin, Vol. 4, p. 565.

Aplastic Anaemia

Aetiology and Pathology

C. P. Rhoads and D. K. Miller studied the histology of the bone marrow in aplastic anaemia by means of sternal marrow puncture. On histological evidence they divided the condition into 5 groups. The first of these was myelophthisic anaemia in which the haemopoietic tissue was replaced by a cellular structure composed of megakaryocytes in various stages of development. In the second group the bone marrow was sclerotic, and in the 3 other groups the marrow cells were either aplastic, active, or hyperplastic. The condition can be compared with agranulocytosis in that impaired maturation of the haemopoietic cells at an early stage is a common histological feature.

P. Emile-Weil described and collected cases, including those of familial infantile pernicious anaemia (Fanconi's syndrome, 1927), of aplastic infantile familial myelosis with malformations and endocrine disorders. Reasons are brought forward to show that the condition was not pernicious (Addisonian) anaemia. There were a number of abnormalities, especially of the testes, dwarfism, and obesity. These facts suggest that hypoplasia of the bone marrow is of inherent origin. Benefit was reported from injection of testosterone propionate.

Émile-Weil, P. (1938) *Sang*, **12**, 369.

Rhoads, C. P., and Miller, D. K. (1938) *Arch. Path.*, **26**, 648.

Haemolytic Anaemias of the New-born

Clinical Picture

Erythrophagocytosis.—T. C. Wyatt *et al.* recorded 3 cases of anaemia of the new-born or icterus gravis neonatorum, bringing the number up to 70; in the 3 cases phagocytosis of the red cells by a monocytic type of cell was detected, bringing the number of cases up to 7. The phagocytes were not numerous, and might easily escape notice; in fact in one of the 3 cases it was not recognized until re-examination of the smears was made 2 years later after attention to the phenomenon had been aroused by a later case. It was suggested that this phagocytosis was not so rare as the recorded cases might suggest. The alternatives that the phagocytosis was due to a fundamental variation in the functional activity of the monocytic cells or of the erythrocytes was discussed, but left open.

Wyatt, T. C., Cooper, M. B., and Groat, W. A. (1938) *Amer. J. Dis. Child.*, **56**, 1319.

Acholic Jaundice

Clinical Picture

R. Debré *et al.* of Paris analyse the clinical features in 37 cases in 14 families of congenital and familial haemolytic disease in children, which they have seen since 1926. In this condition, often called acholic or chronic haemolytic jaundice,

there may be absence of jaundice; this was so in 10 of the 37 cases; a division may be made into (i) the complete type with jaundice, anaemia, and splenomegaly, which is common in adults but less frequent in children and the aged, (ii) non-icteric types. The name 'haemolytic disease' was therefore adopted rather than a designation including the word 'jaundice'.

Anaemia, though more frequent than jaundice, may also be absent, and is usually slight; in one case only was there a red blood count below 3 millions, and in 7 cases it was consistently between 4½ and 5 millions. During acute haemolytic crises with fever, however, the count may fall to 2 or even one million. The well-known increased fragility of the erythrocytes to hypotonic saline solutions varied. In 75 per cent of the red blood-cells their size was diminished (microcythaemia). An increased reticulocyte count was considered of high diagnostic value. Arikín's method of sternal puncture showed an erythroblastic reaction. Increased bilirubinaemia was constant, and a low cholesterolaemia almost so. Splenic enlargement occurred in all the cases. A little known sign was enlargement of the lymphatic glands, ascribed to myeloid transformation. Disturbances of growth and infantilism were not unusual; in 4 cases bony changes were present; in uni-ovular twins there was thickening of the skull bones somewhat resembling oxycephaly, regarded as due to over-activity of the bone marrow. A rare ocular lesion—a white film of the cornea almost filling the palpebral fissure—was composed of nacreous more or less concentric spots and gave the impression of being a deposit; the slit lamp showed that the epithelium was intact. An abdominal syndrome with violent pain and vomiting might imitate appendicitis. Death was rare, the chief danger being febrile anaemia in the haemolytic crises. The transmission of the disease according to Mendel's law was confirmed. Splenectomy, the only efficient treatment, was performed in 6 cases with one fatality.

Debré, R., Lamy, M., Sée, G., and Schrameck, G. (1938) *Amer. J. Dis. Child.*, **56**, 1189.

ANAESTHESIA

See also Vol. I, p. 472, Cumulative Supplement, Key No. 60; and pp 25 and 163 of this volume.

Choice of Anaesthetic

N. F. Heath, in a series of clinical observations on a number of patients anaesthetized with nitrous oxide and oxygen and with ethyl chloride and ether, found that patients anaesthetized in the upright sitting position exhibit a rise of systolic blood pressure in 99 per cent of cases, and a rise of diastolic blood pressure in 95 per cent. In supine or semi-supine patients anaesthetized with nitrous oxide and oxygen the systolic pressure rose in 91 per cent of cases, and the diastolic pressure in 88 per cent. The readings of systolic and diastolic blood pressures, pulse pressure, and pulse rates with the patient in the supine and the semi-supine positions were in each case slightly lower than records taken with the patients sitting upright.

The consensus of opinion is that in dental surgery nitrous oxide and oxygen anaesthesia is superior to ethylene and oxygen, or ether anaesthesia, for the safety and comfort of the patient. Chloroform is contra-indicated in dental surgery when the upright position is desired. Endotracheal inhalation anaesthesia, with a wide-bore catheter packed around with the long gauze 'scarf pack', has great advantages in dental surgery, since the inhalation of blood and mucus is entirely obviated. Furthermore, the anaesthetist is out of the way, leaving an unencumbered field for the surgeon.

Heath, N. E. (1938) *Med. J. Aust.*, **2**, 594.

Ether Anaesthesia

General Physiological Considerations

Ether convulsions.—During 17 years' experience of anaesthetics H. G. Dodd had never encountered a case of ether convulsions. During the next six months he had 4 cases, a fact which he considered to be significant rather than coincident. His suggestion that atropine is probably the final determining factor in the production of ether convulsions was supported by his experience. Until 1936 he had

administered doses of $\frac{1}{100}$ grain of atropine; from that time onwards he increased the dosage in the majority of adult cases to $\frac{1}{4}$ gr. or $\frac{1}{80}$ gr. and it was during this latter period that his only 4 cases of ether convulsions occurred. Successful treatment consisted of giving an intravenous injection of evipan sodium. He recalls that the routine injection of atropine before operation is a post-war development. The more general use of basal narcotics is recommended, but the necessity for watchfulness in this connexion is stressed.

Dodd, H. G. (1939) *Brit. J. Anaesth.*, **16**, 90.

Vinyl Ether

F. F. Cartwright after employing vinesthene (vinyl ether) anaesthetic mixture for 6 months concludes that uniformly satisfactory results are obtained except in abdominal operations requiring profound anaesthesia. Induction may be from the vinesthene mixture direct, either with an open mask or through a Clover's inhaler. The wisest method is probably to drop the mixture from a chloroform drop-bottle on to a Schimmelbusch mask of gauze, enclosed between two layers of gamgee tissue. The rate of flow is one drop per second for the first half-minute, after which the pace of the flow is increased. Consciousness is lost within 30 seconds, and the cough reflex in 2 minutes. Breathing is quiet and the colour good. With the abolition of the cough reflex a change may be made to open ether for maintenance, because of its stimulating effect. A further change back to the mixture may be carried out just before the commencement of operation. The degree of anaesthesia is lighter than that obtained with ether. It is non-irritant to the lungs and relatively non-toxic. Recovery is rapid, the cough reflex returning within 2 minutes of the anaesthetic being withdrawn. Subsequent vomiting is unusual. Vinesthene mixture may be used for maintenance, following induction by other agents, such as ethyl chloride or gas and oxygen. It has also been used as a supplement to avertin, paraldehyde, omnipon $\frac{1}{4}$ grain and hyoscine $\frac{1}{10}$ grain. The greatest field for its use is probably to be found in ear, nose, and throat surgery. The cough reflex is, in these cases, completely under the anaesthetist's control, and can be abolished or allowed to return within a few breaths. It is also an advantage in prostatectomy when patients under spinal analgesia have not received premedication. It is probably of value in Caesarean section. The quantity of anaesthetic required is small. For induction 4 to 6 fluid drachms should suffice, while for maintenance one fluid ounce per hour is generally sufficient to preserve a light anaesthesia. Not more than one fluid ounce should be measured out for use at any time as vinyl ether cannot, when once poured out of the stock bottle, be left from day to day. The cost is relatively high and it should not be forgotten that it is highly inflammable.

Cartwright, F. F. (1939) *Brit. med. J.*, **1**, 1081.

Cyclopropane

Cyclopropane has been held to be responsible for excessive haemorrhage during operation by many authorities. In an attempt to solve this question satisfactorily, W. Neff *et al.* undertook certain investigations which involved the comparison of splanchnic and peripheral blood-supply changes in animals and humans. The apparatus used consisted of a 10-watt lamp, the intensity of which was regulated by a non-flickering carbon rheostat, a Weston photronic cell, and a Weston D.C. microammeter model. The ear or other translucent vascular area was placed between the source of light and the photo-electric cell. When the blood supply was increased, the area became more opaque to light, and the current output of the photo-electric cell was reduced. Alternatively, decrease in the amount of blood increased the current output of the cell.

It was found that changes in the blood supply occurred during cyclopropane and ether administration, each agent exciting changes peculiar to itself. With cyclopropane the peripheral blood supply appeared to be most influenced and the splanchnic least, the reverse being true of ether anaesthesia. The current output of the photo-electric cell was found to vary with the depth of anaesthesia employed, and its reactions were of such delicacy as to record differences in the same plane of anaesthesia, independent of changes in blood pressure. Impending surgical shock gave similar reactions to the onset of sudden severe haemorrhage.

Neff, W., Stiles, J. A., and Michelson, R. (1939) *Brit. J. Anaesth.*, **16**, 83.

Diothane Hydrochloride*For Urethral Anaesthesia*

J. W. Ferrin studied a series of clinically controlled cases, involving urethral dilatation and urethroscopic and cystoscopic examination and treatment using a 1 per cent solution of diothane hydrochloride as an anaesthetic. He concluded that it was infinitely safer for urethral anaesthesia than cocaine or any other accepted anaesthetic. In 100 cases only 2 mild reactions occurred. The toxicity was found to be one-half that of cocaine, but proportionally the anaesthetic qualities were 10 times as strong. The average length of time required for the anaesthetic to take effect was 10 to 15 minutes. From 15 to 30 c.cm. of 1 per cent diothane hydrochloride solution was injected into the anterior urethra and held there for 5 minutes. At the end of that time it was forced into the bladder, and 5 minutes more were allowed to elapse. A further advantage of this preparation is that there is a period of analgesia lasting for a considerable time, sometimes for several days. Although the use of any anaesthetic in the presence of trauma is dangerous, it is felt that reactions might be less frequent and less severe with the use of diothane hydrochloride than with any other product.

Ferrin, J. W. (1938) *J. Urol.*, **40**, 666.

Spinal Anaesthesia*Scope and Limitations*

According to F. B. Mallinson, pregnancy contra-indicates spinal analgesia. It is generally agreed that in pregnancy the blood and central nervous system show variations from the normal; the carbon-dioxide-combining power of the blood is diminished, and therefore the carbon-dioxide content of the blood is increased. The reflex irritability of the central nervous system is also markedly increased. For these reasons a greater fall of blood pressure would be expected to occur in the pregnant than in the non-pregnant patient. These considerations suggest the likelihood of trouble arising from the combination of pregnancy and spinal analgesia.

Premedication with neo-synephrin—A series of 163 cases in which neo-synephrin was used in conjunction with spinal anaesthesia was reviewed by R. S. Brunner and G. de Takats. It was found that a subcutaneous injection of neo-synephrin given prior to the induction of spinal anaesthesia prevented a fall in blood pressure. The effect was apparent in either high or low spinal anaesthesia. After the injection, consisting of 0.5 c.cm. of 1 per cent solution, which was made into the deltoid muscle, readings of the blood pressure were taken every 5 minutes and a further injection given if a fall was noted. In 113 low spinal anaesthetics the loss of sensation extended to the umbilicus; in 50 high anaesthetics the level was at the costal margin in 60 per cent, midway between the umbilicus and xiphisternum in 14 per cent, and at the umbilicus in 26 per cent. The administration of neo-synephrin was found to induce bradycardia, which usually lasted as long as the temporary rise in blood pressure, but in some cases it persisted. The rise in systolic blood pressure occurred within 10 minutes following the injection, and in 27 per cent of cases showed an extent of 20 mm. Hg. One patient developed a marked arrhythmia which lasted for 2 hours, the rate being as low as 30 beats per minute. This patient had, however, developed an arrhythmia before coming to operation. A hundred cases, used as controls, were given injections of ephedrine. In these a gradual drop in blood pressure was observed. The pulse rate remained between 70 and 80 per minute. It was concluded that, if hypotension was due to vasomotor palsy and not to a sudden loss of blood volume, neo-synephrin could be depended on to stabilize the blood pressure. Further, it had no stimulating effect on the central nervous system, nor did it increase irritability on the part of conscious patients. It should be used with caution in old and feeble patients, or with those showing signs of myocardial damage, and preferably coupled with atropine. The dose for each injection should not exceed 0.5 c.cm., but may be repeated when necessary. Patients with a persistent cardiac rate below 50 at rest, which is always suggestive of heart block, are not suitable subjects for the drug.

Procaine Hydrochloride (Novocain) Technique

Spinal anaesthesia is associated with the risk of shock from a rapid lowering of the blood pressure, with vomiting and nausea and, until the introduction of Pitkin's method, with the risk of rapid diffusion. J. L. DeCourcy claimed that administration of the minimal dose to produce anaesthesia reduced the effect of a sudden fall in blood pressure and the frequency of vomiting and nausea. He used procaine

hydrochloride with 1 c.cm. of spinal fluid to dilute it, irrespective of the amount of the drug employed, and found that 50 mg. of procaine hydrochloride was the average dose required, though, for operations such as haemorrhoids, 25 mg. sufficed. In all cases the effect of the anaesthetic lasted about an hour whatever dose or dilution was employed. DeCourcy considered that, if hypotension were the only abnormal sign, it was not a contra-indication to spinal anaesthesia, but that the hypotension which followed haemorrhage was.

Brunner, R. S., and de Takats, G. (1939) *Surg. Gynec. Obstet.*, **68**, 1021.

DeCourcy, J. L. (1939) *Arch. Surg., Chicago*, **38**, 287.

Mallinson, F. B. (1938) *Brit. J. Anaesth.*, **16**, 22.

Local Anaesthesia

Pantocain (Decicain)

F. Schoen collected the cases of pantocain intoxication which ended fatally during the 10 years this preparation has been used. Pantocain, *p*-butylaminobenzoyl-dimethyl aminoethanol hydrochloride, is used extensively for local, regional, and lumbar anaesthesia. Pantocain showed many advantages over procaine and percaine, with which it is very closely allied. The anaesthetic action lasts longer, and there are no late infiltrations after injection which sometimes occurred in using percaine. The addition of adrenaline to pantocain reduced the toxicity of the product, and no concentration above 2 per cent should be used. Care must also be taken to prevent intravenous injection of the drug. The author warns against the use of too large a dose in cases in which a small dose is known to be sufficient.

Schoen, F. (1939) *Wien. klin. Wschr.*, **52**, 505.

Basal Narcosis

Premedication

J. D. Stewart pointed out that premedication makes it possible to take full advantage of modern methods of anaesthesia. In reviewing the various effects of inhalation anaesthetics, he showed the importance of reducing the oxygen requirements and lowering the rate of metabolism. By eliminating the anxiety factor, premedication attains the latter objective, and indirectly, the former also. This effect is particularly valuable when narcosis is to be induced by nitrous oxide, in which case, to attain successful anaesthesia, oxygen requirement must be at a minimum. In addition, a smaller amount of anaesthetic is required.

The quiet respiration which results from suitable premedication makes the work of the surgeon easier, especially in abdominal surgery where, when deep anaesthesia is induced, the diaphragm becomes increasingly active with the reduction in intercostal activity. The physiology of respiration, regulated by the type of anaesthesia employed, whether irritant or non-irritant to the lung tissue, is still further modified by the employment of pre-medication. The author argues that this depression of the respiratory centres which is sometimes held to be a contra-indication for basal narcosis is not in itself dangerous or pathological. It merely increases the necessity for an adequate air-way throughout the entire anaesthetic. The answer to this and to anoxaemic conditions lies in the timely and cautious use of carbon dioxide.

For routine premedication the author prefers an omnopon-scopolamine combination to the combined morphine-atropine. Intravenous injections of the barbiturates are also recommended, but individual dosage must be considered. Of the two rectal basal narcotics the author prefers paraldehyde, and recommends its use in children. There is no appreciable fall in blood pressure or delay in the return of reflexes after the operation. In cases of toxic goitre, avertin or omnopon-scopolamine is suggested, with subsequent nitrous oxide anaesthesia. It should be remembered that morphine and omnopon act as direct metabolic depressants, and serve to render a normal metabolic rate subnormal, whereas barbiturates only reduce metabolism when the metabolic rate is heightened by emotional disturbances. The wide application of basal narcotics, used conservatively, would in the opinion of the author appear to be helpful and most desirable.

Barbiturates

Toxic Effects.—G. R. Cameron investigated the toxic effects sometimes caused by small doses of barbiturates—especially nembutal and evipan sodium. He holds that it is inadvisable to give barbiturates, even in small doses, to the subjects of hepatic

disease and cites considerable experimental evidence that hepatic disease enhances their usual action. This might be due to inhibition of some kind of detoxifying mechanism. The more slowly acting phenobarbitone (luminal) or barbitone-sodium (medinal) show no lengthening of the period of action after acute liver damage. The usual effect of nembutal and evipan may be exaggerated in the presence of anaemia or sepsis.

Pentothal Sodium

Thrombosis.—R. T. Paync reports an extensive thrombosis of the superficial veins of the forearm following the injection of 0.5 g. of pentothal sodium (5 per cent solution) into the median basilic vein. By the fifth day after operation the thrombus extended from the radial styloid process to the anterior axillary fold. Resolution commenced on the eighth day, but the vein was still palpable and slightly tender on the seventeenth day when the patient left the nursing home. Pentothal sodium tends to produce thrombosis more than any other barbiturate derivative.

Pentothal Acid

J. S. Horsley recommends pentothal acid as a satisfactory basal narcotic and remarkable for its rapid elimination and calm post-anaesthetic awakening. Pentothal is thio-nembutal with the composition ethyl (1-methyl butyl) thiobarbituric acid. Small doses are mildly sedative, medium doses hypnotic, and large doses anaesthetic; all these doses are anti-convulsant in varying degree. The stage of drowsiness is brief, lasting 5 to 10 minutes, and is characterized by slight ataxia, but mainly by an overpowering desire to sleep. Respiration is diminished in volume by full anaesthetic doses, but practically unaffected in the dosage recommended for basal narcosis. Basal narcosis lasts from 1 to 2 hours and is suitable for the induction of general anaesthesia. In full doses it induces deep sleep, deep regular breathing, absence of corneal reflexes, partial analgesia, and some degree of surgical relaxation. The toxicity of pentothal, given orally or rectally, is about half that of nembutal, the dose proportionately larger, and the rate of excretion more rapid. The author found that, when pentothal acid was the sole pre-anaesthetic agent, the results were very much better when the drug was given in divided doses, e.g., pentothal 8 grains administered three hours before the induction of complete anaesthesia, and the same dose repeated once or twice at intervals of one hour. After 3 hours every patient was in a deep sleep. The colour was good in every case and most patients were definitely flushed. After pentothal acid in divided doses anaesthesia was completed with either pentothal sodium or vinyl ether. The induction was smooth and uneventful. There was no excitement or restlessness during any stage and post-anaesthetic vomiting occurred in only 3 cases.

Trichlorethanol

Trichlorethanol is the alcohol corresponding to the aldehyde chloral. It resembles tribromethanol in structure but contains chlorine instead of bromine. It is thought to be formed in the body from chloral hydrate. G. Lehmann and P. K. Knoefel studied it with a view to using it as a basal anaesthetic. Its action in depressing the nervous system is similar to that of tribromethanol and 'avertin-fluid', but it has a wide margin of safety and is less depressant to respiration. The alkali reserve is lowered but only to the same extent as by other basal anaesthetics. It is excreted in the urine partly unchanged and partly in combination with glycuronic acid. Tolerance is not readily developed. It does not damage or accentuate previous damage of the heart, liver, or kidneys. When it is employed as a basal anaesthetic, it requires less ether to produce loss of reflexes and cessation of respiration than if tribromethanol had been used. Further it is more soluble in water, and more stable than tribromethanol. It therefore seems to deserve a clinical trial.

Sodium Thioethamyl

C. Langton Hewer tested a new basal narcotic, namely, sodium thioethamyl (sodium *iso*-amylethylthiobarbiturate). It is supplied as a yellow powder in 15 g. glass capsules. The powder is readily soluble in water, yielding a clear straw-coloured solution. The manufacturers recommended that the contents of each ampoule should be dissolved in 15 c.cm. of water, giving a 10 per cent solution. The author, however, preferred a 7.5 per cent concentration as this is less depressing to respiration and circulation. The method of intravenous injection and its effects are practically the same as those of pentothal sodium. It contains a sulphur atom in its

molecule and therefore should not be used on patients receiving sulphanilamide preparations.

Cameron, G. R. (1939) *Proc. R. Soc. Med.*, **32**, 309.

Hewer, C. L. (1939) *Brit. med. J.*, **1**, 109.

Horsley, J. S. (1938) *Brit. J. Anaesth.*, **16**, 1.

Lehmann, G., and Knoefel, P. K. (1939) *Amer. J. med. Sci.*, **197**, 638.

Payne, R. T. (1939) *Lancet*, **1**, 816.

Stewart, J. D. (1939) *Brit. J. Anaesth.*, **16**, 41.

General Considerations

Action of Coramine

R. W. Whitehead and W. B. Draper attempted to determine the action of coramine as an antidote for the inhalation anaesthetics and experimented with dogs to find out the effect of this drug after a minimal dose of ether and of chloroform, and its power of resuscitation when there had been a rapidly administered overdose of these agents. It is pointed out that, when using an analeptic, after its brief action the cessation of breathing is actually hastened. This is explained by the fact that the intensification of the activity of the respiratory neurons necessarily increases their rate of oxygen consumption. Successful resuscitation demands that the oxygen supply to the medulla is increased without delay, without which acute anoxaemia and death of the centre quickly follow. It is essential therefore, when injecting an analeptic, to maintain a free air-way and to increase the oxygen content of the inspired air.

In the authors' experiments there was no evidence that coramine increased the speed or ease of respiration in cases resuscitated by artificial respiration and administration of oxygen. It seems indicated that coramine is useful in the lighter levels of narcosis, and stimulates the respiratory centre depressed by ether, avertin, chloral hydrate, and urethane. It was proved that the use of coramine doubled the mortality from an overdose of chloroform. It was ineffective with barbiturates. It is pointed out that the effect of an analeptic upon the circulatory system is of supreme importance, as it is the behaviour of that system which ultimately decides the issue of resuscitation.

Medico-Legal Aspects

H. G. Dodd discusses the legal position with regard to the responsibility of the surgeon and the anaesthetist during the performance of an operation under an anaesthetic and lays stress on the absence of any established legal position, i.e. that there are no definite legal rulings. It must not always be assumed that the surgeon is responsible for the selection of a competent anaesthetist. Dodd's commentary on liability includes the practice of the surgeon who employs the general practitioner to give the anaesthetic, and also the operator in general practice who employs his partner to give the anaesthetic, whether or not either of these has any knowledge of anaesthesia. Dodd feels convinced that a fully trained and qualified anaesthetist would be held entirely responsible for everything immediately concerning the anaesthetic, but would also find himself fully protected by the law.

Dodd, H. G. (1938) *Brit. J. Anaesth.*, **16**, 16.

Whitehead, R. W., and Draper, W. B. (1939) *Surg. Gynec. Obstet.*, **68**, 892.

Combined Methods of Anaesthesia

Cyclopropane and Percaine Spinal Anaesthesia

As the result of 8 years' search for the best anaesthetic for major operations, especially on the upper part of the abdomen, H. Dodd and J. T. Hunter advocated a combination of cyclopropane 'sleep' with percaine spinal anaesthesia (1 in 2,000) from 8 c.cm. for operation on a limb to 16 c.cm. for an operation on the abdomen. The pre-anaesthetic was omnopon $\frac{1}{4}$ grain and scopolamine $\frac{1}{10}$ grain, and coramine 0.86 c.cm. was injected in order to prevent respiratory depression. The cyclopropane was delivered through a Heidebrink continuous-flow machine with a closed-circuit absorber. The circuit was filled two-thirds full of oxygen, and a mask was applied to the patient's face. Cyclopropane was run into the circuit at the rate of 500 c.cm. a minute until the necessary degree of anaesthesia was obtained, the amount generally needed being 1,500 to 2,000 c.cm. In addition to its advantages, such as calm

respiration, a rapid recovery of consciousness, and absence of nausea and vomiting during operation and of post-operative pulmonary complications, it tended to maintain the level of the blood pressure, and when in a few cases the systolic pressure fell to 80 mm. Hg an intravenous injection of $\frac{1}{4}$ grain ephedrine restored the normal level in 30 seconds. Post-operative headaches, which occurred in 5 to 10 per cent of cases, can usually be relieved by aspirin, phenacetin, and caffeine (A.P.C.) tablets with ephedrine $\frac{1}{4}$ grain 4-hourly or by injection of 20 c.cm. of 30 per cent sodium chloride. As post-operative sedatives, morphine $\frac{1}{4}$ grain or heroin $\frac{1}{12}$ grain and coramine 0.85 c.cm. were suitable.

Nitrous Oxide and Oxygen with Pentothal Sodium

G. Organe and R. J. B. Broad recommend a combination of nitrous oxide and oxygen with pentothal sodium for general anaesthesia. Their results are obtained from 236 operations including orthopaedic procedures, oropharyngeal surgery including tonsillectomy, and gynaecological and abdominal operations of all types. The authors advocate pre-operative medication with omnopon, $\frac{1}{4}$ grain, and scopolamine, $\frac{1}{100}$ grain, an hour before the operation. Anaesthesia is induced with 3 c.cm. of a 5 per cent solution of pentothal. A 10 c.cm. or 20 c.cm. Record syringe with an eccentric nozzle is used, the hypodermic needle being inserted into the median cubital vein and the syringe being strapped to the forearm with two strips of $\frac{1}{4}$ inch adhesive tape. McKesson's gas and oxygen machine is then employed. A further injection of 3 to 5 c.cm. is made approximately two minutes before the incision, and subsequently every 5 minutes 0.5 to 2.0 c.cm. are given according to the depth of anaesthesia which is indicated, usually by slight movements of the hand or by the degree of muscular relaxation. In an abdominal operation an injection of 2 c.cm. before opening the peritoneal cavity and again before closing will usually give the necessary relaxation. Tracheal intubation is always carried out before operations on the mouth or throat. Threatened respiratory failure should be treated by artificial respiration with oxygen and 5 per cent carbon dioxide. An effective antidote is coramine 5 to 10 c.cm. injected intravenously. The total dose of pentothal used averages 0.6 g. or roughly a little over half of that needed for similar procedures without nitrous oxide. Vomiting is greatly reduced, and the after condition of patients is better than with any other form of general anaesthesia.

Dodd, H., and Hunter, J. T. (1939) *Lancet*, **1**, 685.

Organe, G., and Broad, R. J. B. (1938) *Lancet*, **2**, 1170.

ANEURYSM

See also Vol. I, p. 501.

Aneurysm of Aorta

Diagnosis

Kymography.—W. G. Scott and S. Moore discuss the assistance given by kymography in differentiating aneurysm from tumour of the mediastinum, substernal goitre, or tuberculosis of the azygos lobe. They consider roentgen-kymography offers the only graphic and objective way of demonstrating expansile pulsation. They draw attention to its limitations, and point out that few aneurysms are so situated that they can be correctly kymographed, i.e. both sides of the aneurysm must be recorded through the same slit in the kymograph. Changes in density during pulsation, however, offer almost as valuable a demonstration of expansile pulsation as the record of changes shown by the ribbing of the outline.

Treatment

Medical.—The immediate indiscriminate use of arsenicals in patients with late syphilis is dangerous. Bismuth therapy, with digitalis, promotes clinical improvement and probably lengthens life. The analysis of a series of 128 electrocardiograms showed that the degree of myocardial damage portrayed by positive electrocardiographic findings ran parallel with the length of life in most patients. In a group with cardiac pain, no electrocardiographic evidence was present to suggest increased frequency of coronary ostial involvement. Kemp has shown that the cardiovascular system can be completely protected in early syphilis by adequate treatment.

Padget, P., Sullivan, M., and Moore, J. E. (1938) *Arch. intern. Med.*, **62**, 1029.

Scott, W. G., and Moore, S. (1938) *Amer. J. Radiol.*, **40**, 165.

Cardiac Aneurysm

Auricular Aneurysm

Gigantic congenital aneurysmal dilatation of the left auricle in mitral stenosis, and pressing on the left bronchus and recurrent laryngeal nerve, is well known. Cases occur, however, without mitral stenosis, and have been ascribed to a local damage of the auricular wall by inflammation spreading from an abscess in the adjacent and adherent lung, or by multiple emboli; this local 'aneurysmal dilatation', described by Lutenbacher (1918), differed from the less rare and general dilatation in mitral stenosis. J. H. Semans and H. B. Taussig reported a congenital aneurysmal dilatation of the left auricle in a five-year-old child; this was regarded as due to a congenital malformation, and as the first recorded case.

Semans, J. H., and Taussig, H. B. (1938) *Johns Hopk. Hosp. Bull.*, **63**, 404

Aneurysm of the Pulmonary Artery

Shadows of increased density within cavities following haemoptysis have almost invariably been considered to be due to unexpelled blood clot. B. P. Stivelman and M. Malev draw attention to a case of Rasmussen aneurysm, i.e. an aneurysm resulting from a dilatation of a terminal artery in a tuberculous cavity, and believe that a differential diagnosis between this condition and blood clots should be possible. They point out that dense shadows in pulmonary cavities arising from clots will change in size, shape, contour, and position, and will tend to disappear under observation. Shadows due to aneurysmal dilatation would not show these changes if examined by serial radiography. The practical importance of this differentiation lies in the assistance it might give in deciding the form of treatment. The induction of pneumothorax is usually delayed, in cases of haemoptysis, until the blood spitting has ceased. It would appear that this procedure should not be followed in a case of haemorrhage from a Rasmussen aneurysm, as it would tend to result in extensive bronchogenic spread, or exsanguination might occur. In these cases the best interests of the patient would be served by early collapse, in spite of an active haemoptysis and a questionable condition of the other lung.

S. W. Jennes records a case of diffuse aneurysmal dilatation of the pulmonary artery and both of its branches. The infrequency of this condition is shown by figures for the Johns Hopkins Hospital and St Bartholomew's Hospital. No cases were reported in 14,523 necropsies at the former, and 13,324 necropsies at the latter hospital. He reviews the reports of 122 cases of aneurysm of the pulmonary artery, and states that 11 only disclosed a condition similar to his case. Clinical recognition of the condition occurred in 12 out of the 122 cases, the rest being discovered at necropsy.

Jennes, S. W. (1936) *Johns Hopk. Hosp. Bull.*, **59**, 133.

Stivelman, B. P., and Malev, M. (1938) *J. Amer. med. Ass.*, **110**, 1829.

Peripheral Aneurysm

Of the Internal Carotid

Treatment.—T. Rowland Hill has reported 2 cases of leaking congenital intracranial aneurysm successfully treated by ligature. Both cases showed signs suggestive of leaking intracranial aneurysm. Thorotrast was injected, and the position of the aneurysm localized radiographically. Both cases showed aneurysms of the internal carotid, and ligature resulted in relief of pain, and considerable improvement in the 3rd nerve palsy, which had been a noticeable feature in both cases. A third case was described in which a left 3rd nerve palsy was followed by pulsating exophthalmos on the right side, which disappeared in six weeks. A large aneurysm was shown by thorotrast at the termination of the left internal carotid artery. Ligature resulted in recovery. The prevention of the possible development of subsequent hemiplegia and aphasia was discussed, and it was advised that the surgeon should clamp the artery for several minutes before ligaturing; if no hemiplegia occurred, he should proceed with the operation.

Hill, T. R. (1937) *Proc. R. Soc. Med.*, **31**, 215.

ANGINA PECTORIS AND CORONARY THROMBOSIS

See also Vol. I, p. 547, and Cumulative Supplement, Key No. 62.

Angina Pectoris*Aetiology*

According to O. v. Zimmermann-Meinzingen, angina pectoris is due to partial acute ischaemia of the myocardium. It is connected with coronary insufficiency, but is not constant in coronary insufficiency. The main causes of angina pectoris are sclerosis of the coronary vessels, acute coronary thrombosis, high blood pressure, syphilis, gastro-intestinal disturbances, valvular insufficiency, paroxysmal tachycardia, abuse of nicotine, severe anaemia (endocarditis, myocarditis, pericarditis), and toxic goitre.

G. E. Beaumont and J. D. Robertson described the case of a man, aged 44, suffering from attacks of precordial pain, diagnosed as angina of effort. A basal metabolic rate of -33 , despite the absence of any suggestive symptoms or signs, suggested a diagnosis of myxoedema. Adequate thyroid treatment was followed by disappearance of the pain and return to work. The basal metabolic rate rose to -1 , and a return of the symptoms necessitated further hospital treatment and omission of thyroid. Since then, health has been well maintained, and pain had completely disappeared with thyroid $\frac{1}{2}$ grain every third day. The optimal basal metabolic rate in this patient seemed to be between -10 and -17 . This history proves that hypothyroidism, caused by myxoedematous changes in the cardiac nerve-cells and myocardium, produces anginoid symptoms which are relieved by thyroid, and that after thyroid overdosage the same pain might recur, and be caused by spasm or sclerosis of the coronary arteries.

F. Laessing, in reporting 6 cases of nicotine poisoning due to excessive smoking, pointed out a special predisposition to chronic nicotine poisoning in neurasthenics, in persons with unbalanced hormonal secretion, and in alcohol and coffee addicts. The use of English and American cigarettes with 2 per cent of nicotine and rapidly smoked is more likely to cause nicotine poisoning than is that of Continental cigarettes which contain 0.3 to 0.5 per cent of nicotine only. The symptoms of nicotine poisoning resemble those in cardiac neuroses and angina pectoris. They include palpitation, extrasystoles, tachycardia, restlessness, vertigo, headache, pain in the left shoulder and arm, coldness of the extremities, pulse generally slow (35 per minute) and only seldom increased in rate. The electrocardiogram shows signs of change in the frequency and rhythm disturbance of the bundle of His and damage to the heart muscle. Auriculo-ventricular block is characteristic.

Clinical Picture

Angina of effort—An investigation to determine the electrocardiographic changes in angina of effort with special reference to information gleaned from Lead IV was made by G. Bourne and C. Evans. Of 80 cases investigated, 14 showed no changes suggestive of coronary disease in Leads I, II, and III, but definite abnormality in Lead IV. Changes due to a recent coronary thrombosis were excluded from the series, as also were cases of valvular disease of the heart and syphilitic aortitis. In Lead IV—the apical lead—in the earlier records the right arm electrode was placed on the apex-beat and the left arm electrode between the angle of the left scapula and the spinal column, but later the left arm electrode was placed on the outer border of the apex-beat and the right arm electrode on the left leg. The changes indicating myocardial disease in Lead IV were: inverted or diphasic T-wave; an absent initial wave or one of 3 mm. or less; T-wave of high voltage greater than 14 mm.; depression of ST complex of 2 mm. or more. Methods I and II showed little difference in the results obtained. Of the 14 cases with abnormality in Lead IV, T-wave inversion was present in 9 and diphasic T-wave in 2. The initial wave was absent in 2, and in another case the wave never exceeded 2 mm.

Diagnosis

Electrocardiography.—C. L. C. Van Nieuwenhuizen *et al.* selected 350 electrocardiograms from 5,500 curves to illustrate certain changes in the curve due to coronary diseases. They refer to the Q-wave in Lead III as found by Pardee, the occurrence of W- or M-shaped complexes in Lead I or II, and of depressed or elevated ST-segments. These three indicate coronary sclerosis or disturbances

in the blood supply of the coronary arteries. The authors found that, in 84 per cent of cases in which a 'Pardee-Q' was found, clinical evidence of coronary sclerosis existed. In 64 per cent of the cases other electrocardiographic signs besides the 'Pardee-Q' were found. M- and W-shaped ventricular complexes indicated coronary sclerosis in about three-quarters of all cases. If, in a case with M- or W-shaped ventricular complex, there was no coronary sclerosis, some other heart condition (rheumatic, syphilitic, or thyrotoxic) could be found. The so-called positive S-wave or notch at the foot of the RS-wave indicated coronary sclerosis in 85 per cent of the cases. It may be found in other heart affections on a diphtheritic, rheumatic, or syphilitic basis. The thoracic lead and deviations also indicate coronary sclerosis. There is a similarity of the C I and C II types and a deep Q IV which are characteristic.

The 'Cuff-Test'.—S. Robertson and L. N. Katz in a paper on 'Referred pain of cardiac origin', describe a new diagnostic method which they call the 'cuff' test. This consists in the inflation of the usual blood-pressure cuff to 50 mm. above the systemic blood pressure, and keeping it at this pressure for 5 minutes, or until cardiac pain was elicited in the unexpectant patient. The latter was considered a positive 'cuff' test. It was negative in 25 control patients.

93 patients were tested; 80 per cent of the patients with definite angina gave a positive result, while this was only given in 17 per cent of the patients tested by exercise tolerance tests.

They suggest the mechanism involved may be due to one of the following:

- (1) Reflex vasoconstriction of coronary arteries.
- (2) Psychogenic trigger reaction, i.e. the pain in the ischaemic arms sets up the entire syndrome in susceptible individuals.
- (3) A spatial summation of stimuli from heart and forearm using a final common path to the site of pain perception: thus converting a sub-threshold stimulus into a threshold stimulus.

Treatment

Thyroidectomy.—G. Bourne and J. P. Ross reported 12 cases in which severe pain of organic heart disease was treated by thyroidectomy; 9 were improved, 2 had ended fatally, and 1 had not been benefited. Thyroidectomy should not be universally used for patients with cardiac pain but should be reserved for those in whom a classical picture of angina of effort was present, the pain was so severe as to incapacitate the patient, and the clinician was convinced that it was growing worse. Patients with very advanced cardiovascular diseases were not suitable subjects. The after-treatment must be carefully controlled. Patients who underwent total thyroidectomy slowly became myxoedematous, and if given too much thyroid extract had a return of the pain. The aim was to give them the smallest amount of thyroid extract upon which they are able to maintain a comfortable existence. The average intake of thyroid in this series was about $\frac{1}{2}$ grain 5 times per week. The patient was the best judge of the dose.

Two hypotheses had been proposed to account for the relief of pain following the operation: (i) the basal metabolic rate was so lowered that the cardiac burden was relieved; (ii) Weinstein and Hoff considered that during thyroidectomy branches of the superior and middle cardiac nerves of the sympathetic and the superior cardiac rami of the vagus were divided. Another possible hypothesis was that thyroxine sensitized visceral nerve-endings to stimuli, such sensitivity being in proportion to the amount of circulating thyroxine. This accorded with the diminution in pain which follows cessation of thyroid extract. Total thyroidectomy was a difficult operation and care must be taken to avoid including the recurrent laryngeal nerve in a ligature.

Beaumont, G. E., and Robertson, J. D. (1939) *Lancet*, **1**, 682.

Bourne, G., and Evans, C. (1938) *Lancet*, **2**, 1354.

— and Ross, J. P. (1938) *ibid.*, **2**, 815.

Laessing, F. (1938) *Med. Welt*, **12**, 1485.

Pardee, H. E. B. (1930) *Arch. intern. Med.*, **46**, 470.

Robertson, S., and Katz, L. N. (1938) *Amer. J. med. Sci.*, **196**, 199.

Van Nieuwenhuizen, C. L. C., Hartog, H. A. P., and Matthijssen, E. (1939) *Acta med. scand.*, **98**, 468.

Weinstein, A. A., and Hoff, H. (1937) *Surg. Gynec. Obstet.*, **64**, 165.

Zimmermann-Meinzingen, O. v. (1938) *Wien. klin. Wschr.*, **51**, 1301.

Coronary Thrombosis

Pathology

A. M. Masters *et al.* of the Mount Sinai Hospital, New York, analysed the disturbances in intraventricular conduction observed in 375 cases of acute occlusion of the coronary arteries with reference to their incidence, clinical and electrocardiographic features, prognosis, and pathogenesis. All records in which the Q R S interval was prolonged to 0.12 second or more were considered; these included all forms of bundle-branch and intraventricular block, and numbered 57, or 15 per cent, 48 being males and 9 females with an average age of 59 years, as compared with an average of 55 years in the remainder of the 375 cases. Defective intraventricular conduction was commoner in patients who had had previous attacks of coronary obstruction than in those with a first attack. Necropsies on 20 cases showed that defective intraventricular conduction was the same whether the right or the left coronary artery was occluded; in 16 hearts one or more coronary arteries had been previously blocked, and in 16 hearts there was infarction of the interventricular septum. Intraventricular or bundle-branch block was usually associated with considerable enlargement of the heart. Clinically defective intraventricular conduction was usually associated with long-standing hypertension, cardiac enlargement, and congestive heart-failure, the respective incidence of each being 77, 84, and 92 per cent. In the 57 cases left bundle-branch block occurred in 51 per cent, typical or atypical right bundle-branch block in 28 per cent, and intraventricular block in 21 per cent; the last was often associated with impaired auriculo-ventricular conduction. Other arrhythmias were not more common than in ordinary coronary occlusion. Defective intraventricular conduction made the prognosis more grave; in the 57 cases the mortality was 42 per cent as compared with 23 per cent in the remainder of the 375 cases. The treatment did not differ from that of coronary occlusion in general; the use of digitalis and quinidine should be avoided except in the presence of persistent rapid ventricular rate with cardiac failure. Aminophylline intravenously was recommended as sometimes life-saving. Stress was also laid on the value of oxygen, diminished fluid intake, and a low calorie diet.

Diagnosis

Radiology.—G. Levene *et al.* present radiographical criteria for diagnosis of coronary disease, especially occlusion, without knowledge of the history, physical findings, or electrocardiographic records. The normal rate of the heart during fluoroscopic examination being 100 per minute, suspicion should be aroused by a rate of only 50 or 60. In coronary occlusion there is a localized diminution of systolic-diastolic excursion, a loss of convexity of the left heart border due to diminished muscle tone and involutionary myocardial changes, and an increase in the transverse diameter of the heart. Of 140 cases in which a radiological diagnosis of coronary disease was made, confirmatory electrocardiograms were obtained in 103 (76 per cent). In 10 cases in which radiography was carried out on account of precordial pain, no recognizable cardiac disease was found, a fact confirmed by the electrocardiogram. Of 12 cases in which both X-ray examinations and electrocardiograms were made, necropsy confirmed the X-ray diagnosis in 10 and the electrocardiographic in 11. The authors conclude that a radiographic diagnosis of coronary disease is possible in persons without any history of angina and with a normal electrocardiogram.

Treatment

Heparin.—D. Y. Solandt and C. H. Best working with experimental animals consider that the formation of thrombi and resulting cardiac infarction may be prevented by the administration of adequate amounts of highly purified heparin. They emphasize that the main difficulty in the way of the clinical investigation of its therapeutic possibilities in acute coronary crises is the absence of premonitory signs of these conditions.

Levene, G., Lowman, R. M., and Wissing, E. G. (1938) *Amer. Heart J.*, **16**, 133.

Masters, A. M., Dack, S., and Jaffe, H. L. (1938) *Amer. Heart J.*, **16**, 283.

Solandt, D. Y., and Best, C. H. (1938) *Lancet*, **2**, 130.

ANGIOMA

See also Vol. I, p. 577, and Cumulative Supplement, Key No. 64.

Pathology

Association with Hepatic Disease

D. H. Williams and A. M. Snell have recently observed 6 cases of pulsating angioma and hepatic disease at the Mayo Clinic. Parkes Weber first noted the pulsating central eminence of the angiomatous portion which the authors state is the centre of radiating telangiectatic vessels. A prominent feature of the distribution is the occurrence of lesions on the nasal and buccal mucosa. Slight trauma, particularly to the nasal lesions, may give rise to alarming haemorrhage. The familial tendency present in some cases has resulted in the condition becoming known as familial haemorrhagic telangiectasia. The associated hepatic disease is usually chronic, and cirrhosis and splenomegaly are common. Arsenic, alcohol, and syphilis are the common aetiological agents. Two cases of familial hepatic cirrhosis with angioma have been recorded, but the familial tendency is not so marked. In most cases the angiomas appear first and may antedate the hepatic condition by many years. With the onset of the hepatic condition, the cutaneous lesions often increase rapidly in size and number. Partial regression may occur with improvement of the hepatic disease. In all, 15 cases of these associated conditions have been recorded; of these 6 were men, and 9 women. The cutaneous 'spider' type of lesion usually antedated the hepatic disorder. Alcohol was a feature in 3 cases, syphilis in 1, and pulmonary tuberculosis in 1. The authors suggest that the cutaneous manifestations should be looked upon as indicating candidates for hepatic disease, and arsenic and alcohol interdicted.

Williams, D. H., and Snell, A. M. (1938) *Arch. intern. Med.*, **62**, 872.

Treatment

Radiation Therapy

M. Strandquist contends that, as the principal indication for the treatment of haemangiomas is cosmetic, this should be logically supplemented by therapy aiming at their entire disappearance without scarring or cutaneous atrophy. He bases the method described on the vast material of the Radiumhemmet in Stockholm, where radium treatment has been the method used since 1909. The gamma-ray therapy was used exclusively on the 300 cases occurring in 1936-7. Cosmetic restoration almost always occurs after a single radium treatment given within the first 3 months of life. The maximal average dose in 1 cm. superficial tissue is 800 r. Haemangiomas covered by sensitive skin are subjected to an average dose of 700 r, those covered with dense skin are given 850 r. Paling, blanching, and diminution in size are the immediate results, and no further treatment is necessary. If amelioration is not quite so marked, a further course of half the previous dose is given. The author describes the applicators and radium containers used in the Radiumhemmet.

Strandquist, M. (1939) *Acta radiol., Stockh.*, **20**, 185.

ANKYLOSTOMIASIS OR HOOKWORM DISEASE

See also Vol. I, p. 587.

Clinical Picture

H. Hoff and J. A. Shaby reported 2 cases of peripheral polyneuritis associated with ankylostomiasis. One case also showed anaemia, oedema of the wrists and ankles, tachycardia, and a low blood pressure, thereby resembling the polyneuritis due to beri-beri. The patient responded well to treatment with the usual doses of carbon tetrachloride, and the anaemia responded to iron, campolon, and betaxin fortis. The other case was similarly treated, and improved. In it the bisulphite-binding substances in the blood were raised, indicating a vitamin B₁ deficiency. The diet of both patients was in no way deficient in vitamins. It was therefore suggested that the polyneuritis was due to vitamin B₁ deficiency caused by the presence of anky-

lostoma in the bowel; after the infestation and the anaemia had been dealt with, the polyneuritis responded to vitamin B₁ therapy.

Hoff, H., and Shaby, J. A. (1939) *J. trop. Med. (Hyg.)*, **42**, 157.

Treatment

Diet and Vitamin Therapy

In an endeavour to raise the low haemoglobin caused by the anaemia resulting from hookworm disease, prior to de-worming the patient, A. McKenzie administered to 2 patients a high protein and vitamin diet supplemented by dried brewers' yeast. This had little or no effect on the anaemia, but benefited the accompanying general weakness and oedema. Betaxin had a pronounced diuretic effect, which strongly suggested that deficiency of vitamin B₁ was responsible for the oedema.

Medical Treatment

K. P. Hare and S. C. Dutta undertook the investigation of 188 coolies who received treatment for hookworm infection. Of these, 101 cases were given oil of chenopodium, 17 receiving 20 minims and 84 receiving 30 minims, and 87 were given tetrachlorethylene. It was found that the latter drug was infinitely more successful, and that a single dose produced 48.3 per cent of absolute cures as against 4.8 per cent when using oil of chenopodium. 'Absolute cure' was said to result when a stool obtained 14 days after administration of the anthelmintic contained no eggs. Further advantages of tetrachlorethylene were its non-toxicity, only one debilitated female in this series suffering from vomiting and giddiness; its palatability; its simple method of administration consisting of one single dose, shaken up with a saturated solution of sodium sulphate given in the early morning with the patient fasting, and its low cost which is half that of the standard dosage of oil of chenopodium. In a community where mass anthelmintic treatment is required tetrachlorethylene would appear to be the drug of choice.

Hare, K. P., and Dutta, S. C. (1939) *Indian med. Gaz.*, **74**, 198.

McKenzie, A. (1939) *Lancet*, **1**, 1143.

ANOREXIA NERVOSA

See also Vol. I, p. 598; Cumulative Supplement, Key No. 67; and p. 45 of this volume.

Diagnosis

Anorexia nervosa may clinically so closely resemble Simmonds's disease that a differential diagnosis cannot be made until the emaciation and other symptoms disappear as the result of feeding.

Bruckner, W. J., Wies, C. H., and Laviates, P. H. (1938) *Amer. J. med. Sci.*, **196**, 663.

ANTENATAL CARE

See also Vol. I, p. 601; Cumulative Supplement, Key No. 68; and p. 29 of this volume.

Pathology of Mammary Gland during Gestation

R. Bourg discussed the pathology of disturbances of the mammary glands during gestation which are correlated with the intricate endocrinology of the gestational period. Massive hypertrophy or macromastia was often observed in the early stages of pregnancy; the bilateral appearance helps to distinguish the condition from other enlargements of the breast. Radiotherapy and injections of human milk intramuscularly (5 c.cm. daily) were successful in treating the condition.

Adenomas and fibroadenomas often develop during gestation; being benign they need not be treated until after pregnancy is terminated. Aberrant mammary glands were occasionally found in the axilla, where they were thought to be apocrine glands; their enlargement and secretion during gestation is the chief point in diagnosis.

Infections of the mammary gland occur more often during gestation than normally, and it was found that abscesses were more numerous in the winter. Post-partum abscesses are too well known to demand description.

The disturbances of secretion are important; agalactia and hypogalactia occur in a number of cases. Injection of progesterone and folliculin (oestrone) is necessary to correct the hypofunction. Ultra-violet irradiation is often helpful in mild cases. Vitamins must be present in the diet, and vitamin E must be administered in large doses if necessary. Hypergalactia and galactorrhoea, the other extreme which may occur, is treated by mercury salts, such as neptal or salyrgan given intravenously or intramuscularly on two consecutive days, or by oestrone, in doses of 10,000 to 20,000 I.U., treatment being commenced on the third or fourth day. Testosterone can replace the female hormone in the treatment of this condition. Hypersecretion of folliculin was found to produce adenomas in the breasts, and its possible carcinogenic action is being considered. Increased excretion of folliculin by the urine demands a close investigation of the breasts.

Bourg, R. (1939) *Gynec. et Obstét.*, **39**, 427.

Hygiene of Pregnancy

Diet

E. V. McCollum confirms the fact that the basal metabolic rate in pregnancy falls very slightly during the first months and thereafter steadily rises until a few days before delivery when it is 23 per cent above the figure 5 months earlier. The daily iron requirement, which has been assumed to be 15 mg. for the normal adult, is more than 20 mg. for the pregnant woman. The response to iron therapy is much increased when the diet contains an abundance of fresh fruit and vegetables. The author states that, in this condition, ferric salts are of more value than ferrous, since the latter destroy vitamin A. The recent tendency to force a high carbohydrate diet on patients with vomiting of pregnancy is viewed with caution, and the author supports the view of Berkwitz and Lufkin who consider that the nerve changes in pregnancy are similar to those resulting from infective conditions and dietetic deficiency disturbances such as beri-beri.

McCollum, E. V. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 586.

ANUS DISEASES

See also Vol. I, p. 643, and Cumulative Supplement, Key No. 71.

Anal haematoma

Treatment

E. E. Arnheim described his technique for the removal of external and internal haemorrhoids by the use of the high-frequency electric current. Any diathermy machine producing a steady unipolar current was found to be convenient. The length of the spark is usually $\frac{1}{4}$ inch. An electrode, devised by Wappler, and capable of taking any straight sewing needle, was used in the 189 cases treated by this means.

Epidural anaesthesia produced by a 1 in 1,500 procaine solution, or low spinal anaesthesia with 90 mg. of procaine, was used. The largest external haemorrhoid was grasped with Allis clamps and pulled outwards, thus exposing the internal haemorrhoid, and a haemorrhoidal clamp was applied to the base of the mass. After certain preliminary preparations the haemorrhoidal mass was destroyed by first applying the spark to the entire surface until the latter became greyish white. After this the needle was plunged into the mass several times until it was reduced to a small greyish piece of coagulated tissue. The mass was then removed from the base of the clamp with the high-frequency current, and the remaining tissue on the clamp thoroughly coagulated. The clamp should be removed slowly, notch by notch, to avoid haemorrhage. Of this group of 189 patients, follow-up proctoscopic examinations were performed in 156 cases during a period of 1 to 6 years, and two small and insignificant recurrences of internal haemorrhoids were found. There were no deaths or post-operative strictures in the whole group.

Arnheim, E. E. (1938) *Amer. J. Surg.*, **41**, 45.

Pruritus Ani*Aetiology*

A. Castellani described a state of pruritus due to fungi, usually trichophyton-like fungi and yeast-like fungi. Common throughout the tropics and subtropics, it might also occur in the temperate zone. The fungi might be secondary invaders. Coliform bacilli, *B. mucosus*, *B. proteus*, and various cocci had also been found. The bacteria probably cause a secondary eczematous dermatitis but it was doubtful if they caused the pruritus. The monilial form was commoner in females than in males and was probably due to vaginal discharge containing monilia derived from infection of the peri-anal and anal regions.

Castellani, A. (1938) *J. trop. Med. (Hyg.)*, **41**, 377.

APPENDICITIS

See also Vol. I, p. 729.

Clinical Picture*Leucocyte Count*

In a published report on the significance of a low leucocyte count in acute pyogenic infections C. H. Watson and T. R. Sarjeant concluded from the total leucocyte count and the polymorphonuclear count in acute appendicitis (160 cases, divided into groups according to the conditions, mild, severe, abscess, generalized peritonitis) that a low leucocyte count indicated, not a failure on the part of the bone marrow in leucopoiesis, but the withdrawal of a large number of leucocytes from the blood stream to a suppurating focus. In the ordinary acute appendicitis one of the earliest signs of infection was a rise in the leucocyte count, the curves of the total leucocyte count and the polymorphonuclear count running parallel; when the peritoneum was involved, there was a further rise in the polymorphonuclear count, with an increasing shift to the left, due to the entry of young leucocytes into the blood; but there was an abrupt fall in the total leucocyte count, the extent of the fall being determined by the size of the area involved in the suppurative process. In fatal cases the curves representing the total leucocyte and the polymorphonuclear counts diverged continuously; whereas when the infection was successfully resisted, the curves converged and fell together to normal. In lobar pneumonia the white counts behaved in the same way; in uncomplicated cases the counts rose rapidly, remained high during the acute stage, and fell together with recovery; in pneumonia complicated by empyema the total leucocytes showed an abrupt fall, whereas the polymorphonuclear count remained high. In the obstructive form of appendicitis described by Wilkie which was not primarily infective but more closely allied to acute intestinal obstruction, there might not be any significant change in the total leucocyte and the polymorphonuclear counts.

Watson, C. H., and Sarjeant, T. R. (1938) *Canad. Med. Ass. J.*, **39**, 460.

Wilkie, D. P. D. (1930) *Canad. med. Ass. J.*, **22**, 314.

Treatment

R. J. McNeil Love discussed the 'appendix mass', especially in connexion with its treatment. It became palpable 48 or more hours after the onset of acute appendicitis, and was due to local peritonitis or, at a later stage, to abscess, with local rigidity and tenderness. There were 2 schools of thought about treatment: (i) Expectant treatment, which was not suitable for children or the aged, consisted in nursing the patient in Fowler's position, fomentations, and other methods of relieving pain. If this method was adopted, 3 events might follow: (a) Subsidence of the local peritonitis and recovery; this occurred in 65 per cent of cases collected by the author. Three months later the appendix was removed. (b) The formation of an abscess; this occurred in 25 per cent of the cases. (c) Increasing local rigidity, raised pulse and temperature rendered imperative abandonment of expectant treatment, and the adoption of laparotomy. This occurred in 10 per cent of the cases undergoing the expectant treatment, and probably had made some surgeons advocate immediate operation. Love was much in favour of the expectant treatment. (ii) Immediate operation might be difficult and spread the infection. Analysis of a

large number of cases showed that the mortality-rate was 6 per cent as compared with 3 per cent among the cases treated by the expectant plan.

Peritonitis

In the treatment of peritonitis attention must be paid to drainage of the peritoneal cavity, abdominal wall (after closure of the parietal peritoneum) and the intestinal lumen. According to F. G. Connell death in appendicitis was not due to appendicitis, but to peritonitis, and death in peritonitis was not due to peritonitis but to ileus. The cause of death in ileus was not established, but was often ascribed to 'toxaemia'. This article is devoted to advocacy of the prevention of ileus, dynamic and adynamic, by drainage of the intestine. If the ileum was drained by operation distension and paralysis could be overcome. In 56 cases in which enterostomy was performed at the time of appendectomy for perforated appendix, when the danger of peritonitis followed by ileus was so great, the mortality-rate was 14.2 per cent, as contrasted with 88 similar cases treated without enterostomy with 13 deaths, 14.7 per cent. These statistics are admittedly of little value on account of varying unknown and inconstant factors. A distinction was drawn between (a) prophylactic ileostomy, which was preferable to caecostomy and was performed at the operation for perforative appendicitis and did not add to the risk, and (b) therapeutic enterostomy which was usually delayed too long and had interfered with the acceptance of prophylactic ileostomy.

Connell, F. G. (1938) *Amer. J. Surg.*, **41**, 255.

Love, R. J. McN. (1939) *Lancet*, **1**, 1253.

Tumours of the Appendix

Carcinoids (argentaefine tumours)

J. E. Porter and C. S. Whelan found, among 26,384 vermiform appendices removed at the Boston City Hospital, Mass., between 1910 and 1937, 84 cases of carcinoids or argentaefine tumours, 72 of the vermiform appendix, and 12 from parts of the intestine; 3 were malignant. It is estimated that a carcinoid tumour is found once in every 200 or 500 appendices. The tumour is described as potentially malignant, but of a low grade. From examination of the published papers, 18 previously untubulated malignant carcinoids have been found; this brings the total number of recorded malignant cases up to 67.

Porter, J. E., and Whelan, C. S. (1939) *Amer. J. Cancer*, **36**, 343.

ARGYLL ROBERTSON PUPIL

See also Vol. II, p. 6.

Pseudo Argyll Robertson Pupil

P. H. Heersema and F. P. Moersch found records at the Mayo Clinic during the 23 years ending January 1, 1938, of 57 cases of Adie's syndrome. Any evidence of syphilis, encephalitis, or organic nervous disease precludes this diagnosis. It is usually stated that this syndrome, which is entirely benign, is 4 times commoner in women than in men, but in their cases there were 32 females and 25 males. This pupillary change is usually unilateral, and may be associated with absence of deep tendon reflexes, but the authors considered that absence of tendon reflexes, particularly ankle-jerks, is too frequent to have any serious diagnostic or prognostic significance. The aetiology is still unsettled, but there is much to be said for the view that a disorder of the autonomic nervous system is operative. The condition is often associated with a tendency to frequent emotional disturbance and vasomotor lability. The sharpest point of differentiation from the true Argyll Robertson pupil is the delay in reaction to convergence exhibited in Adie's syndrome as contrasted with the brisk response in neurosyphilis. The treatment consists mainly in simple reassurance and explanation of the benign nature of a pupillary change which has been ascribed to neurosyphilis.

Heersema, P. H., and Moersch, F. P. (1939) *Proc. Mayo Clin.*, **14**, 17.

ARRHYTHMIA

See also Vol. II, p. 10, and p. 59 of this volume.

Extrasystole*In Children*

Extrasystoles occur in children in both diseased and healthy hearts. R. A. Lyon and L. W. Rauh examined a large number of children to determine the incidence of extrasystoles and to find, if possible, the predisposing factors and the effect of the cardiac irregularity on the health of the children. They found them in 35 out of 782 children attending clinics for cardiac diseases; in 3 of 5,114 newly born infants; in 40 of 1,782 children having some cardiac abnormality; and in 7 of 709 children in a single elementary school. The irregularity occurred in 2.2 per cent of normal hearts and 4.3 per cent of cardiac lesions. The electrocardiograms of 22 children showed them to be of ventricular origin in 16 cases, of nodal origin in 3, of auricular origin in 3, and multifocal in 1. In most cases no cause for the extrasystoles could be found though some showed such aetiological factors as rheumatic fever, congenital heart disease, and emotional and nervous instability. There was no evidence in this series that extrasystoles in themselves are harmful or retard the growth or development of the child.

Lyon, R. A., and Rauh, L. W. (1939) *Amer. J. Dis. Child.*, **57**, 278.

Tachycardia*Treatment with Quinidine*

B. A. Gouley and L. Soloff discuss the administration of quinidine in the treatment of arrhythmia and tachycardia caused by digitalis. In 1 or 2 cases they report that this treatment was strikingly successful in arresting a serious cardiac arrhythmia due to digitalis poisoning. Twenty grains of quinidine were given in 4 equal doses by mouth during a period of 24 hours. A marked slowing of the heart rate followed. Ultimately normal sinus rhythm was restored. Their failure in the second case they ascribed partly to inadequate dosage, and partly to the advanced state of cardiac decompensation present in that patient. The administration of quinidine is contra-indicated, particularly in the presence of marked cardiac enlargement and congestive failure.

Gouley, B. A., and Soloff, L. (1938) *Amer. Heart J.*, **16**, 561.

Bradycardia*Heart-Block*

Treatment with Cardiazol—H. C. Lueth reviewed four cases of complete heart-block with the Adams-Stokes syndrome. Each was treated by cardiazol (metrazol). Cardiazol acts promptly after subcutaneous injection; its use in circulatory collapse is well known. Of the 4 cases reported by Lueth, 2 were greatly benefited by the drug and 2 were not. It is believed that the beneficial effect of metrazol in complete heart-block with Adams-Stokes syndrome is due to its vasomotor and respiratory stimulative action.

Treatment with Paredrine—Paredrine (*p*-hydroxyphenylisopropylamine), which stands between adrenaline and ephedrine in chemical structure, was found by M. H. Nathanson to have a beneficial effect on heart-block, and to increase ventricular function, without exerting the unpleasant effects which may result from the use of ephedrine. The drug is stable and can be administered effectively by mouth. Its effect was more prolonged than that of adrenaline, and there were no signs of central nervous stimulation. Its action on the electrocardiograph was similar also to that of adrenaline, the RT segment being depressed in 4 out of 12 cases and the T wave being increased in amplitude in 7.

In some cases a comparatively lengthy cardiac standstill was induced by pressure on the right carotid sinus, thus causing an intense vagal stimulation. By this means the sinus node becomes inactive and cardiac standstill occurs, and there is no impulse initiation from secondary centres. Paredrine was administered in 14 such cases, in 12 the oral dose being 60 mg. and in two 40 mg. The cardiac standstill was modified in every case, being abolished in 7 by the development of a rhythm arising around the auriculo-ventricular node as revealed by the electrocardiogram. Similar devia-

tions were observed in the electrocardiogram after the administration of paredrine and of epinephrine.

Lueth, H. C. (1938) *Amer. Heart J.*, **16**, 555.

Nathanson, M. H. (1939) *Ann. intern. Med.*, **12**, 1855.

Auricular Fibrillation in Infancy

Treatment

M. Goldbloom and H. N. Segall reported a case of auricular fibrillation which was diagnosed in a female infant of 3 months, but had probably been present from birth. Soon after birth the infant was noted to have tachycardia and arrhythmia. She also had cyanosed and cold extremities, and grunted with each breath. She could not tolerate quinidine sulphate, but responded to digitalization which was started at the age of 3 months.

Goldbloom, M., and Segall, H. N. (1938) *Amer. J. Dis. Child.*, **56**, 587.

ARTERIAL DISEASE AND DEGENERATION

See also Vol. II, p. 39, and p. 61 of this volume.

Periarteritis Nodosa

Actiology and Clinical Picture

J. W. Kernohan and H. W. Woltman found that out of about 200 cases of periarteritis nodosa 15 per cent had been diagnosed clinically or by biopsy. It had been suggested that it was due to a virus of the 'rheumatic group'. The age incidence was between 3 months and 78 years, and men are four times more often affected than women. The mortality was said to be 90 per cent. The various organs are affected as follows: kidneys in 80 per cent, the heart in 70 per cent, the liver in 65 per cent, the gastro-intestinal tract in 50 per cent, the mesenteric arteries in 30 per cent, the muscles in 80 per cent, the nerves in 20 per cent, and the central nervous system in 8 per cent. Leucocytosis occurs in 32 per cent; although eosinophilia strongly suggested the diagnosis of periarteritis nodosa, it was present in 12 per cent. Neurological symptoms were emphasized in this article; they were often prominent, the peripheral nerves being much affected. When the cranial nerves were attacked, blindness, diplopia, facial paralysis, deafness, and dysphagia might result; and involvement of the central nervous system might cause headache, vertigo, tremor, chorea, convulsions, hemiplegia, delirium, and coma. The disease had been mistaken for trichiniasis, myositis, purpura haemorrhagica, amoebiasis, hepatic abscess, miliary tuberculosis, meningitis, cerebral tumour, alcoholic neuritis, and lead neuritis. Remissions and exacerbations are characteristic of the disease.

Associated eye changes.—A. Gjertz *et al.* described a case of periarteritis nodosa in which episcleritis was observed in the right eye in the last month of the patient's life, corresponding to the contralateral lesion of similar description established during the last year. On admission to hospital nothing abnormal was found in the patient's eyes, but some time later his vision deteriorated, and ophthalmoscopic examination revealed two greyish spots with diffuse borders resembling foci in miliary tuberculosis. The rest of the clinical symptoms were typical of the condition, namely, chronic pyrexia, marked anaemia with leucocytosis and relative eosinophilia, polyneuritis, and haemorrhages from the urinary and digestive tracts. The authors published this case, as it appears to be the first observation of eye changes in periarteritis nodosa.

Gjertz, A., Nordlöw, W., and Svenmar, M. (1939) *Acta med. scand.*, **100**, 310.

Kernohan, J. W., and Woltman, H. W. (1937) *Proc. Mayo Clin.*, **12**, 554.

Thrombo-Angiitis Obliterans (Buerger's Disease)

Actiology

Neither the formation of a thrombus nor the presence of infection explain all the clinical phenomena of thromboangiitis obliterans. Koga in 1913 believed that the changes in the vessels were secondary to increased viscosity in the blood and since

then many attempts have been made to treat the condition by diluting the blood. F. V. Theis and M. R. Freeland investigated the blood changes in 7 cases of acute thrombo-angitis obliterans. They examined superficial venous blood from the affected leg, and found increased viscosity, rapid coagulation, and raised sedimentation-rate. The cell counts were normal or low. The alkalinity of the blood was greatly increased with a high oxygen saturation and low carbon dioxide content. When the clinical condition improved, the oxygen saturation rose and the blood count increased, in some cases to polycythaemia. The authors deduced from these observations that a disturbance of the use of oxygen in tissue metabolism was one of the conditions responsible for the acute symptoms of thrombo-angitis obliterans. They suggested that examination of the blood could be used for early diagnosis, to detect recurrences, and to show when the disease has been arrested.

In a review of 948 cases of thrombo-angitis obliterans observed at the Mayo Clinic over 30 years, B. T. Horton found that 28 per cent of the patients were Jews and 72 per cent Gentiles; 98 per cent were men. The same chronic occlusive arterial phenomena were present in all cases with strikingly similar clinical picture and course. The mean age of the men was 42 years and of the women 38. Of the patients in the series, 93 per cent were cigarette smokers. Of the 948 patients 401, i.e. 33.6 per cent of the Jewish patients and 45.6 per cent of the Gentiles, underwent amputation either at the clinic or elsewhere, 85 undergoing bilateral amputation. One third of the amputations were of a minor character, i.e. amputation of a toe or finger.

Prognosis

A study of amputations by B. T. Horton for 3-, 5-, and 10-year periods after the onset of the disease indicates that approximately 70 per cent of patients will survive for 3 years from the onset without the necessity of amputation, 60 per cent for 5 years, and only 40 per cent for 10 years. Sympathectomy, though not curative, is the most logical surgical procedure for increasing the blood supply. Of the 948 patients, 175 are known to be dead, coronary disease being the commonest cause of death (27 per cent).

Treatment

Alcohol injections.—M. Pavone described the successful treatment of a case of thrombo-angitis obliterans by injection of alcohol into the splanchnic nerves on both sides. Many cases have been described in the literature in which splanchnic resection has effected marked improvement in the symptoms of peripheral arterial disease, as in Raynaud's disease, Buerger's disease, and juvenile gangrene. The author studied the question of chemical neurolysis, and concluded that the injection of absolute alcohol into the splanchnic nerves gave the same results as the resection of the nerves. The technique used was to anaesthetize the site of puncture and the deeper tissue in the area of the 12th dorsal vertebra, and to push the needle in obliquely towards the vertebral body, starting from about 1 inch from the side of the spinous process. At a depth of about 4 inches the injection was made. On the left side care must be taken not to puncture the renal artery, and therefore the injection was made a further half-inch laterally.

Horton, B. T. (1938) *J. Amer. med. Ass.*, **111**, 2184.

Pavone, M. (1939) *Cultura med. mod.*, **18**, 71.

Theis, F. V., and Freeland, M. R. (1939) *Arch. Surg., Chicago*, **38**, 191.

Chronic Arteritis

Aetiology

H. T. Karsner investigated the thickness of the aortic media in hypertension in 420 aortae which were divided into groups according to age and sex, and correlated with the blood-pressure records made in life. The middle coat of the aorta increases in thickness as age advances; this is accompanied by increase in the space between the elastic lamellae, and the media is thicker in males than in females. The media is most probably affected in hypertension in the same way as by the ageing process. The changes in the media of young hypertensive subjects resemble precocious senile changes.

Karsner, H. T. (1938) *Trans. Ass. Amer. Phys.*, **53**, 55.

ARTHRITIS

See also Vol. II, p. 65, Cumulative Supplement, Key Nos. 94-102; and p. 135 of this volume.

Gonococcal Arthritis*Treatment*

Sulphanilamide.—H. C. Coggeshall and W. Bauer discussed the treatment of gonococcal arthritis with large doses of sulphanilamide. The cases included proved gonococcal arthritis with and without infected synovial fluids and patients suffering with rheumatoid arthritis. Administration of the drug was continued over 2 or more weeks, and efforts were made in all cases to maintain a high level of sulphanilamide in the blood, i.e. 10 mg. per cent or over. It was found that the infected synovial fluids could be sterilized in 48 to 72 hours after institution of therapy; and in 17 out of 18 cases having a proved genito-urinary focus, no gonococci were found after the third day of treatment. The results in 14 proved and 4 probable cases of gonococcal arthritis were more satisfactory, and occurred sooner than in other forms of therapy. The authors stated that the best results were obtained in cases in which treatment was commenced before joint destruction had begun. Cases of rheumatoid arthritis did not respond to sulphanilamide administration and, in contrast to cases of gonococcal arthritis, the erythrocyte sedimentation rate remained unchanged in the majority of cases. Toxic results of this therapy were easily recognizable and were not serious.

A. Cain *et al.* treated a male patient suffering from gonococcal arthritis and ophthalmia with sulphanilamide. Six days after contracting gonorrhoea, the patient had pain in his left knee, fever, and, soon afterwards, pain in the right knee and ankle also, and symptoms of inflammation in both eyes, especially of the conjunctiva. The patient received daily for 5 days a dose of 5 g. of the drug orally. The urethral symptoms were much improved, the eye symptoms, however, became worse, and the arthritis was not influenced at all. The temperature remained high. The drug treatment was interrupted, and a shock treatment with antidiphtheritic serum was tried, without success. Eventually, 1 c.cm. of a solution of sulphanilamide containing 0.25 g. was injected into the knee joint after 10 c.cm. of fluid had been removed by puncture. The temperature subsequently fell. A second and third injection each of 2 c.cm. of the solution were given; the temperature fell to about normal; movement of the joint was now possible without pain, and the swelling disappeared. The eyes also improved, but a scar remained on the right cornea.

Cain, A., Cattani, R., and Arnous, J. (1938) *Bull. Soc. méd. Hôp. Paris*, 3^e sér., **54**, 1733.

Coggeshall, H. C., and Bauer, W. (1939) *New Engl. J. Med.*, **220**, 85.

Rheumatoid Arthritis*Diagnosis*

Injection of vital azo dye.—The vital azo dye, T-1824, or Evans blue, which has been used in estimation of blood-plasma volume, and is known to pass through inflamed, but not through healthy, capillaries has been found by M. S. Burman and D. H. Kling to pass, after intravenous injection, into the synovial fluid of patients with active rheumatoid arthritis. It was suggested that this procedure may be of use in estimating the activity or the latency of the changes in rheumatoid joints. The method entailed aspiration of the joint or arthroscopy.

Treatment

Gold therapy.—S. J. Hartfall *et al.* tested the use of parmanil in rheumatoid arthritis; this is a methyl glucamide of auro-thio-diglycolic acid with a total gold content of 50 per cent. It is put up as a 5 per cent and a 2 per cent oily suspension. It is injected intramuscularly at weekly intervals, a course generally consisting of 12 doses. From an initial injection of 0.5 c.cm. of the 5 per cent suspension (0.025 g.) the dose is gradually raised to 2 c.cm. (0.1 g.). The results are as good as, if not better than, those achieved over a long period with 4 other gold salts—lopion, solganal B oleosum, crisalbine, and myocrisin. The average amount of gold salt per course in the parmanil-treated cases was 0.6 g., whereas the average amount of gold salt per

course in other cases was more than 1 g. It is also the gold preparation with the minimal toxic reactions; these occurred in approximately 25 per cent of cases.

Cinchophen.—During an investigation into the relation between cutaneous sensitivity, hepatic function, leucopenic index, and the toxic effects of cinchophen, W. B. Rawls found that the production of urticaria by the administration of cinchophen relieved arthritic symptoms in 5 out of 9 cases. The total cinchophen given in these 5 cases, over varying periods, ranged from 90 to 315 grains. The author considered that jaundice did not normally become visible until the icterus index was 20 or 25, the normal index being 4 to 8. In the cases quoted, the highest icterus index after administration of cinchophen was 12.5, and there was no visible jaundice at any time. Urticaria appeared in from 4 to 14 days after the commencement of treatment, and relief from pain, swelling and stiffness of joints occurred either at the onset of the urticaria or after its subsidence. The periods of relief varied from 3 weeks to 5 months, an average being 9 weeks. It was concluded that cinchophen toxicity involved various chemical reactions and that the one responsible for urticaria was not necessarily that which brought about good results in arthritis. This view was supported by the fact that 4 patients who received cinchophen and developed severe urticaria failed to gain any relief from the arthritic symptoms.

Sulphur and iodine.—E. Fletcher treated chronic arthritis with sulphur and iodine. Sulphur detoxicates both chemical and bacterial poisons in the body. Indole, a product of tryptophane, has been found in excess in the urine of arthritic patients, and it disappears on their recovery; normally it breaks down into indoxyl and then combines with sulphur to form indican (potassium indoxyl sulphate). Carbohydrates may take the place of the sulphur-containing proteins in the diet, but an acute exacerbation has been known to follow a high carbohydrate diet in rheumatoid arthritis (Fletcher, 1922), and sulphur has therefore been often combined with a low-carbohydrate diet. Sulphur is wide-spread in the body, and, using the cystine content of the nails as an index, it has been shown that there is less sulphur in the older patients with rheumatoid and mixed arthritis and that sulphur is of the greatest value in these cases. Atherosclerosis does not occur so commonly in races, such as the Japanese, whose diet contains a high content of iodine. Possibly iodine plays an important part in sulphur metabolism, because cystine is stated to be oxidized by iodine, probably to cysteic acid. Colloidal sulphur was injected into 5 patients with rheumatoid arthritis, 15 with osteoarthritis, and 5 with fibrositis. The initial dose was 1 c.cm. for the rheumatoid arthritis and 2 c.cm. for the other types. A severe reaction occurred after the second dose in some rheumatoid patients, and a few only of these were slightly improved. The results were better in osteoarthritis, and those with fibrositis all got well. The osteoarthritic patients were divided: (i) chiefly women in the 4th to 7th decades of life with essential hypertension and (ii) with obesity. In the first group 15 out of 30, and in the second group 8 out of 26 patients treated with iodine (French tincture, and later ammonium *ortho*-iodoxybenzoate, and calcium *ortho*-iodoxybenzoate) became free from symptoms, and others were improved. Sulphur and iodine were combined in the treatment of chronic arthritis; 20 c.cm. daily for one week followed by 40 c.cm. for a second week, of a preparation of sodium iodide and magnesium tetrathionate ($\text{S}_4\text{O}_6\text{Mg}$) were injected intravenously into 20 patients: 4 became free from symptoms, 12 were improved, and there were 4 failures.

Vitamin D.—The administration of massive doses of vitamin D in rheumatoid arthritis is, according to N. R. Abrams and W. Bauer, of little or no value in altering the course of the disease. Out of 18 cases so treated, 8 only experienced subjective relief lasting throughout the period of treatment. In 3 instances only was this accompanied by objective improvement and in only one was it impressive. Even this was short-lived when treatment was discontinued. The general effects of the larger doses were not significantly different from those with the usual doses.

Therapeutic jaundice.—P. S. Hench drew attention to the observation made by various authors, and by himself, on the remarkable effect of jaundice on patients with atrophic rheumatoid (chronic infective) arthritis. A spontaneous remission in the symptoms of arthritis and fibrositis occurred when the patient became jaundiced due to an intercurrent intrahepatic jaundice such as epidemic infective and cinchophen jaundice, or an obstructive jaundice such as that due to gall-stones or malignant growths; the remissions lasted approximately 2 or 3 times the duration of the jaundice. This led him to speculate on which factors characteristic of icterus were responsible, so as to be able to build up a treatment on this basis.

It had at different times been suggested that bilirubin, bile salts, a hepatic

autolysate, a special diet, simple sedation (i.e. non-specific reduction of pain due to toxins), counter-irritation, dehydration, or even rest and reduction of the trauma might be responsible for this remarkable effect. Investigations were also carried out to discover the mechanism by which the effective agent acted, and it was thought that jaundice altered the chemical composition of fibrotic arthritic tissues or that hepatic damage temporarily reduced the production of some substance of which rheumatic patients had an over-supply. It had also been thought that the agent possessed detoxicating, bacteriolysing activity. All these investigations proved to be unsuccessful and the therapeutic jaundice which was artificially produced did not lead to uniform results. The failure, however, was due to the mildness of the icterus produced by toluylenediamine, by transfusion of highly jaundiced blood, or by the other substances used to induce icterus. Following the hyperbilirubinaemia induced by intravenous injection of bilirubin and decholin as carried out by H. E. Thompson and B. L. Wyatt, bilirubin was injected by Hench in large doses, 15 mg. per kilogram of body weight daily during periods varying from 6 to 30 days, and in half the 12 patients short incomplete improvement was observed. The author concluded that, though this was a promising research, it did not justify the exploitation of bilirubin and bile salts for the treatment of arthritis at present.

Abrams, N. R., and Bauer, W. (1938) *J. Amer. med. Ass.*, **111**, 1632

Burman, M. S., and Kling, D. H. (1939) *Acta rheumatol.*, **11**, 1

Fletcher, E. (1939) *J. R. Inst. publ. Hlth.*, **2**, 104

Hartfall, S. J., Garland, H. G., and Goldie, W. (1938) *Lancet*, **2**, 1410.

Hench, P. S. (1938) *Arch. intern. Med.*, **61**, 451.

— (1938) *Brit. med. J.*, **2**, 394.

Rawls, W. B. (1939) *J. Amer. med. Ass.*, **112**, 2509

Thompson, H. E., and Wyatt, B. L. (1937) *J. Amer. med. Ass.*, **109**, 481.

Osteoarthritis

Treatment

Gold therapy and diet—J. A. Key *et al* treated 70 patients with chronic proliferative arthritis (osteoarthritis) with myocrisin (sodium aurothiomalate); all were chronic cases who had received various treatments before gold therapy was instituted. The myocrisin was given intramuscularly into the deltoid or gluteal regions. The initial dose was 0.05 g. and one week later 0.1 g. was given. This dose was continued for 20 weeks until the patients had received 2 g. of myocrisin or 1 g. of gold. After a first course of treatment, 6 weeks' rest was given. Then, if the disease was still active or if the sedimentation-rate was raised, a second series of injections was given. If a third course was necessary, an interval of 4 to 6 months was allowed to elapse.

In addition the patients were given a full diet supplemented with large doses of vitamin C. To those with anorexia and constipation, vitamin B₁ was given, and to those who were underweight, a high calorie diet. The patients when possible were ambulant, but they were advised not to get overtired, and many of them were given special exercises. Salicylates were prescribed when necessary for pain. Of the patients, 44 developed toxic symptoms such as dermatitis, albuminuria, and fever. The gold was stopped at once, and complications were treated symptomatically. The patient was rested for 4 weeks before resuming treatment and if toxic symptoms again appeared, treatment was abandoned. There were no deaths. In 3 of the cases of proliferative arthritis the disease was arrested, in 18 there was marked improvement; in 13 the improvement was moderate, and in 4 slight. In the remaining 56 cases there was no benefit, or the patients did not return for observation, and in 2 cases the disease was aggravated. In 9 cases of spondylitis ankylopoietica the treatment did not result in sufficient improvement to warrant its continuance. In 4 cases in which the proliferative arthritis appeared to be gonococcal there was little or no beneficial effect. In 2 cases of lymphogranuloma the arthritis was not improved, but the rectal condition of one of the patients showed marked progress while under gold therapy.

Key, J. A., Rosenfeld, H., and Tjoflat, O. E. (1939) *J. Bone Jt Surg.*, **21**, 339.

Chronic Infective Arthritis

C. A. Robinson and V. C. Robinson consider that cervicitis is a common focus of infection and a definite pre-arthritic condition. It is often noted that arthritic

symptoms date from the time of marriage, or from a confinement or miscarriage. The initial symptoms are backache, pelvic tenderness, mild parametritis, and excoriation of the cervix with subsequent development of joint pains. Fifteen cases are reviewed, 11 being chronic infective and 4 of the rheumatoid type.

Treatment must be primarily of the cervical condition and consists of intra-pelvic diathermy. It is found that the chronic infective type responds more satisfactorily than does the rheumatoid, and that a fall in the sedimentation rate accompanies improvement in the arthritis. The authors emphasize that true menopausal arthritis must be distinguished from chronic infective arthritis occurring at that time, and from osteoarthritis. Menopausal arthritis should also be treated by intra-pelvic diathermy, aided by the application of infra-red rays to the affected joints (usually the knees), and passive movements and exercises.

Robinson, C. A., and Robinson, V. C. (1938) *Brit. J. phys. Med.*, N.S. 1, 340.

Treatment of Different Types

It was pointed out by C. W. Scull *et al.* that chronic arthritis presented a variety of symptoms involving deviation from normal protein metabolism. Some of the extra-articular phenomena involved disturbances from the normal course of protein metabolism.

The authors presented a statistical analysis of the levels of total protein, albumin, globulin, and the albumin-globulin ratios in a series of 177 patients with various types of rheumatoid disease. Slight reductions in the albumin levels were observed in a number of severe atrophic, hypertrophic, and mixed cases. Severe atrophics presented increased globulin levels and decreased albumin-globulin ratios. Atrophic spondylitis is characterized by a high level of total proteins and a lower albumin-globulin ratio.

It was concluded that therapeutic measures incorporating an optimal supply and balance of nutrients, protection of inflamed or irritated tissue, removal of sources of infection and toxæmia are essential to a fundamental approach to arthritis, whatever the categorical type presented.

Gold Therapy

R. G. Snyder *et al.* treated 100 cases of arthritis with gold therapy. This group was subdivided into 50 cases of rheumatoid arthritis, 20 of osteoarthritis, and 30 with mixed arthritic infections. Gold sodium thiosulphate (sanocrysin) was the preparation used in the majority of cases, and intravenous injections were given twice a week for 6 weeks. A period of 6 to 8 weeks was allowed to elapse between the first and second courses, and this was increased by one month between each successive course of treatment. In some cases sulphhydryl gold naphthyl trisulpho-carbonium (auricein) was given intramuscularly, to replace the intravenous injections of sanocrysin. Toxic reactions occurred in 17 patients, in 11 of whom skin rashes were the main feature. Gastro-intestinal disturbances occurred in some cases, and one case of oedema involving the epiglottis required tracheotomy. Improvement was noted in 41 per cent of the entire number, made up of 24 from the rheumatoid group, 9 from the osteoarthritic, and 8 from the mixed group. The necessity for standardization of gold preparations and of dosage is emphasized, and it is suggested that gold therapy should only be instituted when other forms of treatment have failed. The initial dose was 5 mg. If no toxic reactions developed, the dose was increased by 5 mg. gradually to 100 mg., the total dosage in a series approaching 1,000 mg.

Dangers.—P. Lagère warned against the indiscriminate use of the salts of gold or other heavy metals without a proper control of the elimination of the preparation. He specially attributed to oily suspensions cumulative effects which may, in some cases, appear only after 2 years. He reported a clinical history in which a patient who had received chrysotherapy for arthritis with complete success one year previously, developed intense prurigo, oedema, myocardial degeneration, and painful patches all over the body, starting with ulcerative stomatitis. Sodium thiosulphate was used in treatment, and only prolonged efforts succeeded in curing the patient. The author finally emphasized the necessity of examining the blood gold-level and the elimination in the urine during chrysotherapy.

Sulphonamide drugs.—F. Coste *et al.* described favourably the treatment of rheumatic joint conditions by drugs of the sulphonamide group. They originally used the hydrochloride of sulphamidochrysoidine, probably in inadequate dosage, but

more recently they changed to M & B 693. They emphasize the necessity of giving large doses. Arthritic conditions are far more resistant to treatment than other conditions, as is shown by the experience of urologists who found that gonorrhoea was easily controlled by sulphonamides, but that gonococcal arthritis required far larger doses before success was obtained. The authors advocate the intra-articular injection of M & B 693, in addition to the oral method. Out of 56 cases treated, the results were as follows. (i) Of 13 cases of gonococcal arthritis, 10 were cured. The three failures were hypersensitive to the sulphonamide preparation. (ii) There were 43 non-gonococcal cases, and of these 23 were either cured or much improved. It is to be emphasized that only chronic or subacute cases were treated, as the risk of hypersensitivity and more serious complications (agranulocytosis) is present. An average of 50 to 100 grams of M & B 693 was given within one month, and the majority of patients tolerated this dosage well.

Coste, F., Gaucher, M., Morin, M., and Guiot, G. (1939) *Bull Soc. méd. Hôp. Paris*, 3^e sér., **55**, 702

Lagèze, P. (1939) *Pt. méd.*, **47**, 864.

Scull, C. W., Bach, T. F., and Pemberton, R. (1939) *Ann intern med.*, **12**, 1463.

Snyder, R. G., Traeger, C., and Kelly, Le M. (1939) *Ann intern med.*, **12**, 1672.

Arthritis in Children or Still's Disease

Aetiology

Atkinson analysed 86 complete cases of Still's disease, namely those with the pathognomonic triad—enlargement of the joints, spleen, and lymphatic glands—described by G. A. Still in 1897. A list of 32 cases is given in which one or more of this triad were absent and of doubtful nature. In 84 cases 48 were males and 36 females, the usual age at onset being between 2 and 5 years, the youngest child was 4 months old. In 10 cases a bacterium, especially *Streptococcus viridans*, had been found either during life or at necropsy. In nearly all cases there was anaemia. In 35 of the 86 cases the liver was enlarged.

Atkinson, F. R. B. (1939) *Brit. J. Child Dis.*, **36**, 100

ASCARIASIS

See also Vol. II, p. 146

Clinical Picture

B. Zohn investigated the question as to whether in pregnant women hypersensitivity to *Ascaris lumbricoides* was transmitted across the placenta. Intracutaneous injections of 0.05 c cm of extract of *Ascaris lumbricoides* were given to 12 non-sensitive pregnant women. At the birth of the infants, the mothers' blood was tested and in 9 reagins were present, but in blood taken from the umbilical cord they were absent.

A case of acute haemorrhagic pancreatitis associated with ascariasis is described on p. 455.

The possible relationship between anaemia due to intestinal worms and the components of the gastric juice, particularly Castle's intrinsic factor, is discussed on p. 558.

Zohn, B. (1939) *Amer. J. Dis. Child.*, **57**, 1067.

ASCITES

See also Vol. II, p. 153.

Ascites with General Oedema

Ayerza's Disease

Aetiology.—E. E. Smith discussed the clinical syndrome, known as Ayerza's disease, which is characterized by chronic cyanosis, dyspnoea, erythraemia, and pulmonary sclerosis. Smith reviewed the literature and, on the basis of a case seen

in 1937, came to the conclusion that more than one aetiological factor was responsible for the syndrome. Clinical evidence is in favour of a syphilitic origin with primary sclerosis of the pulmonary artery, but other causal agents may also be responsible. The author's patient presented a history of a chronic pulmonary condition with frequent headaches, a characteristic cough, a generalized cyanosis, an evident polycythaemia, and dyspnoea, but no arthritic changes of the fingers. No evidence of syphilis was found.

Smith, E. E. (1939) *J. Pediat.*, **14**, 602.

ASPHYXIA IN CHILDREN

See also Vol. II, p. 173.

Asphyxia Neonatorum

W. Borgard and F. Hoffmann investigated the comparative resistance to asphyxia in the new-born. It was found that new-born animals were far more resistant if there was a lack of the normal percentage of oxygen. It was also found that they survived a negative atmospheric pressure of 720 mm. Hg, whereas fully developed animals die at a negative pressure of 600 mm. Hg. These observations corroborate the statements of Hugget and Haselhorst *et al.* that the foetus *in utero* can survive with an oxygen content which is only 25 per cent of the maternal blood-oxygen. According to the authors this phenomenon is due to the fact that the foetal and new-born organism possesses all the factors which combat asphyxia, i.e. they have a high pulse-rate, a large number of red corpuscles, and a high haemoglobin ratio; also the glutathione and the catalase content of the blood is higher than in the adult. After a short period of extra-uterine existence, however, a change occurs, characterized by a diminution in the number of erythrocytes, decrease of the haemoglobin content, and, as a sequel to the destruction of the red blood-corpuscles, the organism is flooded with bilirubin, which is manifested in the icterus neonatorum so commonly observed.

Borgard W., and Hoffmann, F. (1939) *Arch. Gynaek.*, **168**, 873.

ASTHMA

See also Vol. II, p. 179, and Cumulative Supplement, Key No. 110

Clinical Picture

Eosinophil Counts

Investigations were made in the case of 103 asthmatics—43 males and 60 females—over a period of 9 to 12 months in order to try to account for the divergence which occurs in the blood eosinophil counts of individual asthmatic patients. The information gained was tabulated by H. B. Hunt, but the exact cause for the fluctuations between patients, and in the same patient at different times of the year, could not be found. Furthermore, no differentiation could be established between 'intrinsic' and 'extrinsic', or between infective and non-infective asthmas, on the basis of eosinophil counts. Eosinophilia is quite common in bronchial asthma, but, when large counts are made, the average is usually only a little over 5 per cent. There appears to be some relationship between the blood and sputum eosinophilia. Two hundred and sixty-seven differential white-cell counts were performed, the figures varying between zero and 19.5 per cent.

Hunt, H. B. (1939) *J. Allergy*, **10**, 146.

Diagnosis

Radiography

R. Debré *et al.* studied radiographically the chests of infants and children suffering from asthma. The polymorphism of infantile asthma made this investigation very difficult, and it was found that eosinophilia was not always demonstrable in the patients. Radiologically the thorax was enlarged, the intercostal spaces were wide, and the movements of the diaphragm diminished; the latter sign was always

indicative of the condition. The hilar region was enlarged mainly downwards, and at the height of the attack the transparency of the lungs was also diminished. All these signs were elicited during the attack, as they were found to be transient. They were, however, constant, and the authors expressed their view of the possibility of confirming the diagnosis by this method.

Debré, R., Lamy, M., Mignon, M., and Nick, J. (1939) *Pr. méd.*, **47**, 957.

Treatment

Prevention of Attacks

Insulin—H. Bartelheimer stated that there is a close relation between allergic phenomena and endocrine glandular function. According to recent literature asthma is rare in diabetes mellitus, as are allergic conditions generally. Bartelheimer had previously shown that the anaphylactic effect of serum in guinea-pigs could be diminished or even abolished by a series of insulin shocks, and proved that the effect was due not to some hormonal influence but to the hypoglycaemia, which causes liberation of histamine and related substances which might be partly responsible for the anti-allergic effect. Bartelheimer treated 10 asthmatics by insulin shock, 20 to 50 units of insulin being injected before breakfast. Before the injection, and subsequently at half-hourly intervals, the blood pressure, pulse rate, and vital capacity were measured. On the first morning 20 units of insulin were given, and if symptoms of shock were not produced the dose was increased on subsequent mornings to 30, 40, or 50 units in order to produce the shock syndrome perspiration, trembling, hunger; 15 to 30 minutes later the shock was interrupted by the administration of 40 grams of glucose by mouth. Each patient had 12 shock treatments given at intervals of 2 to 5 days. The beneficial effect could be seen about half an hour after injection. Dyspnoea definitely improved and there was an increase of the vital capacity (30 to 100 per cent). Pulse rate and blood-pressure level were lowered.

M. Langeron *et al.* also employed insulin in resistant asthmatic attacks. They state that this treatment should be reserved for those cases in which all the classical methods of treatment have failed. To produce hypoglycaemia they found 20 to 80 units of insulin were necessary, depending on the initial level of the blood sugar. The results are immediate, the patient soon after the intramuscular injection of insulin begins to exhibit symptoms of hypoglycaemia, such as perspiration, faintness, tremor, loss of consciousness, relaxation of the sphincters, and convulsions. At the height of the hypoglycaemic symptoms, 20 to 30 c.c. of hypertonic glucose solution are injected intravenously; this promptly checks further hypoglycaemia, and the patient recovers quickly, with a retrograde amnesia and voracious appetite. In very resistant cases, 3 or 4 courses are given. After each hypoglycaemic reaction the patients feel much relieved, and dyspnoea disappears completely. The authors suggest a vegetative reaction as the explanation of the phenomenon.

H. Vollmer used a modified form of Sakel's insulin-shock therapy in treating the long-standing asthma of children. The dosage was regulated individually, and varied from time to time in the same patient. The initial dose was generally 5 units, and was increased by 5 units to a maximum of 40 units. Once the shock reaction was obtained the dose was not increased, but it is stressed that a physician should be constantly in attendance, and should himself prepare a solution of sugar water (50 to 100 g.) which should be kept ready for use. Intravenous sugar solution, syringe, and tube-feeding apparatus must also be ready. A series of 15 to 25 subcutaneous insulin injections was given at intervals of 2 days, or, when the attacks were frequent, an injection was given at each attack. Seven children, whose ages varied between 3 and 12, were thus treated. The beneficial effect is ascribed to a secondary endogenous adrenaline production following the administration of insulin. It is suggested that, in severe cases, adrenaline should be replaced by insulin for control of the attacks, thus inducing this endogenous production, rather than causing a possible adrenal hypofunction by constant administration of adrenaline. The injections are given either fasting or 4 hours after the last meal. The insulin reactions begin 30 to 60 minutes later.

Surgical.—Bilateral resection of the posterior pulmonary plexus completely interrupts the extrinsic nerve supply of the lung. The preganglionic efferent fibres of both the vagus and the sympathetic bronchomotor tracts from the same and opposite sides, and the sensory or afferent fibres emerging from the lung, form an anastomosing plexus on the posterior surface of the hilum of the lung. By resection of the

plexus it is possible to remove the lung from any influence brought to bear upon it by its extrinsic nerve supply. W. F. Rienhoff, Jr., and L. N. Gay selected 11 cases of typical asthma in which all medical treatment had failed and in which the patients were incapacitated by their condition. Bilateral resection of the plexus in these patients produced diminution of the attacks, and reduced sputum and emphysema in all cases. After operation smaller doses of ephedrine were necessary to control the remaining attacks. The operation was performed in 2 stages at an interval of a fortnight, and, after the second side had been operated on, the attacks became even less frequent and markedly less severe, in some cases eventually disappearing. No deaths attributable to the operative procedure occurred.

Lumbar puncture.—M. Hochrein and I. Schleicher described 3 patients with bronchial asthma who were favourably influenced by lumbar puncture. Some cases of asthma resist all attempts at treatment, and this led the authors to examine the pressure of the cerebrospinal fluid, as it is known that in cases of reflex neurosis—and asthma is a reflex neurosis—increased cerebral pressure may cause congestion of the lungs. It was found that in cases of asthma pressure was abnormally high, and that, after removal of 10 to 20 c cm. of fluid, all symptoms, such as dyspnoea, pain, and discomfort, disappeared. The authors recalled a former publication in which 5 cases were described, all of which improved after reduction of lumbar pressure. Lumbar puncture, in addition to stopping an attack, improves the mechanism of respiration, an important but neglected factor in bronchial asthma, this is explained by the increased vital capacity obtained after relieving pulmonary congestion.

Short-wave therapy with 'rotating electrode.'—J. P. P. Stock advocated short-wave therapy in the treatment of asthma, employing the rotating electrode which he himself evolved, and for which he claims advantages over the conventional fixed electrode commonly employed. Of the 83 cases so treated 90 per cent have either become completely free from attacks or such attacks, if present, have been trivial. The rotating electrode is placed over the 'nasal bridge' at a distance of 1.5 cm. The posterior electrode is placed 2.5 cm. from the scalp at the 'back of the head'; the leads from the machine are kept at as great a distance as possible from the patient's body, to avoid the possibility of the latter acting as electrodes. Three treatments a week are given, 12 treatments representing a course. During the first week of treatment the patient is instructed to spray his nose each morning with a freshly-made 10 per cent solution of argyrol.

Treatment of Attacks

Adrenaline in oil. The advantage of adrenaline, in the form of a 1 in 500 suspension of the crystalline product in purified peanut oil, in cases of chronic asthma, is that it is more slowly absorbed and has a more lasting effect. In cases in which the usual daily number of adrenaline injections had been from 9 to 12, they were replaced by 3 or even 2 injections of slow adrenaline. An injection frequently enabled a patient to have a comfortable night. A group of 9 cases was thus treated by J. A. Murphy and C. A. Jones, and relief was obtained in every case by the use of this preparation. It is not suggested that the preparation is a cure for asthma, but that it has marked advantages over the aqueous solution. Untoward effects were few, and only one of the 9 treated cases was unable to tolerate slow adrenaline.

Adrenaline and gelatin.—W. C. Spain *et al.* report on a preparation of combined adrenaline and gelatin which possessed the advantage of reducing the number of injections necessary when using the aqueous 1 in 1,000 solution. The gelatin-adrenaline is slowly absorbed, it is non-toxic and non-antigenic, and, as it is given subcutaneously, it may be self-administered. Gelatin-adrenaline contains twice the amount of adrenaline present in the ordinary aqueous solution. Reactions to injections are infrequent, and then are delayed from 20 to 30 minutes. Fifty patients were treated by this therapy, the majority showing improvement in their general condition and in their asthmatic symptoms. The number of injections required by contrast with the aqueous solution was considerably reduced, and exhaustion associated with asthmatic attacks disappeared to a striking degree.

Aminophylline.—G. T. Brown reported the case of a man, aged 74, who for 48 years had suffered from asthma, necessitating the frequent use of asthma powders, adrenaline hypodermically, and other remedies. Skin tests showed that he was extremely sensitive to linseed, and moderately so to ragweed pollen and house dust. After exposure to linseed products he had severe attacks, and became so exhausted that he was admitted to hospital for a week and was given daily intravenous

injections of aminophylline with much benefit. After discharge from the hospital he had a very severe asthmatic attack with cardiac oedema, pulmonary oedema, and coma, and appeared to be moribund; he did not respond to morphine, atropine, and digitalis hypodermically; but, after an intravenous injection of 0.48 g. of aminophylline and 18 c.cm. of 50 per cent sterile dextrose solution, he made a dramatic recovery, and for 4 months was entirely free from asthma. When giving aminophylline for the first time to a patient the dose should not be more than 0.24 g. in 10 c.cm. of distilled water or dextrose solution; it should be injected slowly in order to prevent unpleasant reaction. The oral administration of theophylline combined with ephedrine was useful, and phenobarbitone was recommended in moderately severe attacks of asthma.

Helium and oxygen.—In treating patients with intractable asthma or respiratory obstruction, W. R. Lovelace advises inhalation with, at first, a mixture of 80 per cent helium and 20 per cent oxygen from a single cylinder. With improvement in the patient's condition the flow of oxygen and helium from this tank is gradually decreased, and the flow of oxygen from another tank containing pure oxygen is increased, thus decreasing the percentage of helium. Any recurrence of respiratory distress, increase in the pulse rate, or restlessness, should be the signal for an increase in the percentage of helium until the symptoms have been controlled. The flow of helium and oxygen is adjusted according to the respiratory minute-volume of the patient. Enough of the mixture is allowed to flow into the inhalation apparatus to ensure that the reservoir-rebreathing bag is not quite emptied with each inspiration. At the beginning of treatment all atmospheric air should be excluded by the closure of all port-holes.

Cyclopropane anaesthesia—N. E. Meyer and S. Schotz reported a case of intractable bronchial asthma in which deep surgical anaesthesia was induced and maintained for 10 minutes by cyclopropane. The strain on the cardiac system was relieved, and the necessary relaxation obtained. Upon recovery the patient expectorated, and was treated with steam inhalation and expectorant mixtures, and had no recurrence of asthma during the ensuing 14 days, at the end of which she was discharged from hospital. The authors feel that, in certain cases of bronchial asthma in which all other measures have failed, induction of general anaesthesia, preferably with cyclopropane because of its rapid action and lack of irritation to the respiratory tract, is justified.

Bartelheimer, H. (1938) *Dtsch. med. Wschr.*, **64**, 1254.

Brown, G. T. (1938) *J. Allergy*, **10**, 64.

Hochrein, M., and Schleicher, I. (1939) *Klin. Wschr.*, **18**, 665.

Langeron, M., Cordonnier, V., and Baude, B. (1939) *Bull. Soc. méd. Hôp. Paris*, **55**, 812.

Lovelace, W. R. (1938) *Proc. Mayo Clin.*, **13**, 790.

Meyer, N. E., and Schotz, S. (1939) *J. Allergy*, **10**, 239.

Murphy, J. A., and Jones, C. A. (1939) *J. Allergy*, **10**, 215.

Rienhoff, W. F. Jr., and Gay, L. N. (1938) *Arch. Surg., Chicago*, **37**, 456.

Spain, W. C., Strauss, M. B., and Fuchs, A. M. (1939) *J. Allergy*, **10**, 209.

Stock, J. P. P. (1939) *Brit. J. phys. Med.*, **2**, 32.

Vollmer, H. (1939) *Arch. Pediat.*, **56**, 223.

ATAXY

See also Vol. II, p. 202.

Leyden-Westphal's Acute Ataxy

Leyden and Westphal described cases of ataxy with acute onset. There has been much controversy on the aetiology of this affection, and also as to whether it is an affection *sui generis*. R. Giorgini considers that distinction between primary and secondary acute ataxy seems to be justified only to a certain degree. A review of the literature demonstrates that acute ataxy is different from disseminated sclerosis. Osteomyelitis may be complicated by acute ataxy. Microscopical examination did not definitely explain this syndrome. It probably results from more or less diffuse toxic or infective causes which damaged a congenitally weak system of co-ordination.

Leyden and Westphal (1939) *Note Psychiat., Pesaro*, **68**, 65.

ATHLETICS AND ATHLETIC INJURIES

See also Vol. II, p. 220, and Cumulative Supplement, Key Nos. 114 and 115.

Athletics*The Kidney and Sport*

G. S. Foster enumerated the differences between the urine voided prior to a race and that passed immediately after its completion. It was found consistently in all 18 cases investigated that the latter was darker and that, whereas previous to the run only in 5 cases were the urines slightly cloudy, subsequently in the whole 18 they became so. Of the 13 specimens which had been clear at the start, in 4 cases albumin was present in the second specimen. Ten of the 18 specimens at the end of the race showed an average increase in specific gravity of 6 points. Whereas 17 out of 18 pre-race specimens had been alkaline, afterwards 15 out of 18 were acid. Eleven of the 18 with urines normal prior to the race manifested albuminuria after it. Of 16 who showed no red blood cells in the sediment prior to the run, following it 9 showed them in varying amounts, while 7 did not. Similarly, though 11 had shown no evidence of casts, 9 subsequently showed hyaline and fine granular, short, narrow casts. Running seemed to reduce the percentage of those presenting calcium oxalate crystals.

Foster, G. S (1939) *J. Amer. med. Ass.*, **112**, 891.

Athletic Injuries*Joints*

Treatment of sprains.—E. J. Moynahan treated 17 cases of acute ankle sprain and 9 cases of sprains of other joints (1 wrist, 2 fingers, 2 thumbs, 2 knee, and 2 'back') by Leriche's method which consists of infiltrating the peri-articular tissues with a solution of procaine hydrochloride 0.5 to 2 per cent. In ankle sprains an injection of 10 to 15 c.cm. was usually sufficient. Pain was eased, movement restored, and swelling reduced. Pain subsequently returns and does not finally pass off for 4 to 7 hours. In most cases little disability remains in the affected joint. In some cases the injection may need to be repeated the following day. Occasionally more than 2 injections are required. The 'after-pain' may be great, but is relieved by injections of physiological saline. The average period of incapacity in cases treated by this method was 2 to 3 days instead of the customary 10 to 12.

Injuries to Muscles and Tendons

Crepitating peritendinitis.—N. J. Howard discussed crepitating peritendinitis which he considered an acute pathological condition resulting from prolonged muscular exertion performed after a long period of inactivity. Pathologically the changes consisted of oedema of the peritendinous areolar tissue and muscle, especially involving the junction of muscle and tendon. Thrombosis of the venules was present with deposits of fibrin in the areolar tissue. The muscle may undergo degeneration to the point of necrosis within the sheath. Of 72 cases studied, 91.5 per cent were in men and 8.5 per cent in women; 38 followed direct trauma. The others had no direct evidence of trauma or strain, but all had returned to work or sport after a long absence. Treatment was directed to complete immobilization of the wrist and the fingers, including the thumb, by moulded plaster of Paris splints. In 34 cases so treated, immobilization lasted an average period of 11.6 days only. In 25 cases in which straight board splints were employed and the thumb was left free, the average disability was 22.6 days.

Isolated Rupture of Trochanter Minor

K. Herzog describes two cases of athletic injuries in 2 boys aged 13 and 17 in whom an isolated rupture of the trochanter minor occurred. The epiphysal line of the trochanter minor is in adolescents a *locus minoris resistentiae* in the apparatus consisting of the iliopectineal, femur, pelvis, and spinal column. This *locus minoris resistentiae* changes according to age so that, in the adult, the most vulnerable part is the muscles, and in people over 50 years of age, the skeletal part. The age of patients with an isolated rupture of the trochanter minor in the epiphysal line is almost always less than 18 years. A clinical sign of the injury is typical fracture pain. There is a palpable painful region extending from the ligamentum inguinale to the fossa iliopectinea. There is also sometimes a swelling of this region. Sometimes

walking is nearly impossible; sometimes it is quite normal and nearly painless. One of the main symptoms is the impossibility of lifting the leg in the sitting position, although when lying down the leg can be flexed (Ludloff's sign). There is an inability to stand upon the injured leg, or to climb upstairs. The radiograph shows the rupture or fracture of the trochanter minor. Treatment consists of rest in bed with flexion of knee and thigh. Neither operation nor plaster casts is needed. The prognosis is always good.

Herzog, K. (1939) *Dtsch. Z. Chir.*, **251**, 449.

Howard, N. J. (1938) *Amer. J. Surg.*, **42**, 723.

Moynahan, E. J. (1939) *Brit. med. J.*, **1**, 671.

AVIATION

See also Vol II, p. 239, and Cumulative Supplement, Key No. 116

Examination of Pilots

Hypotension

A. F. Rook and D. J. Dawson investigated the relation between flying and hypotension. The Royal Air Force has for some time regarded as evidence of hypotension a systolic pressure below 110 mm. Hg and diastolic pressure below 70 mm. Hg. Moderate grades are considered to be present if the systolic level is between 110 and 100 mm. Hg, and severe grades when the systolic pressure is below 100 or the diastolic below 60. Of fit pilots serving in the R.A.F. between 1927 and 1931, 3 per cent were hypotensive. Hypotension accompanied by symptoms, such as postural giddiness, is an absolute bar to all flying. It may be occasionally found in a large proportion of young adults when repeated examinations are made. It is rare for hypotension to be persistent and even then it is rarely permanent. Only if associated with symptoms or with some underlying disease, e.g. pulmonary tuberculosis, is it

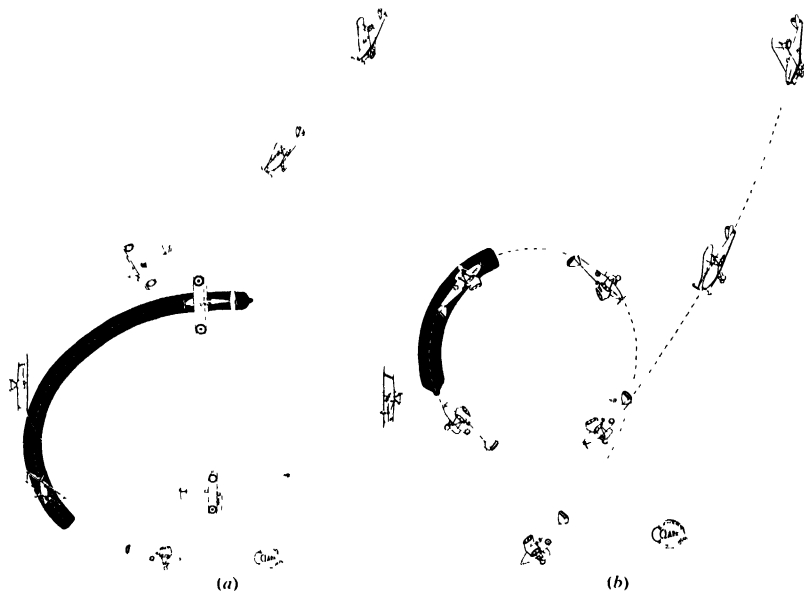


FIG. 9.—(a) 'Black-out' produced by turning sharply at the bottom of a dive. The actual position of the aircraft at each phase of the movement should be observed. Onset of 'black-out' and recovery shown in black. Initial gravity factor, 5 g. (b) 'Black out' effected by a tight loop producing $g = 6\frac{1}{2}$ at 185 m.p.h. Period of blindness shown as in (a).

(This and Fig. 10 from the *British Journal of Surgery*, 1939)

a bar to flying. The ability of the cardiovascular system to withstand centrifugal force during flight depends on its power to react rapidly to stress.

Rook, A. F., and Dawson, D. J. (1938) *Lancet*, 2, 1503

Special Tests for Aerobatics

'Black-outs'

P. C. Livingston investigated the problem of 'black-out' in aviation and recorded his own observations and sensations. He stated that a feeling of intense bodily

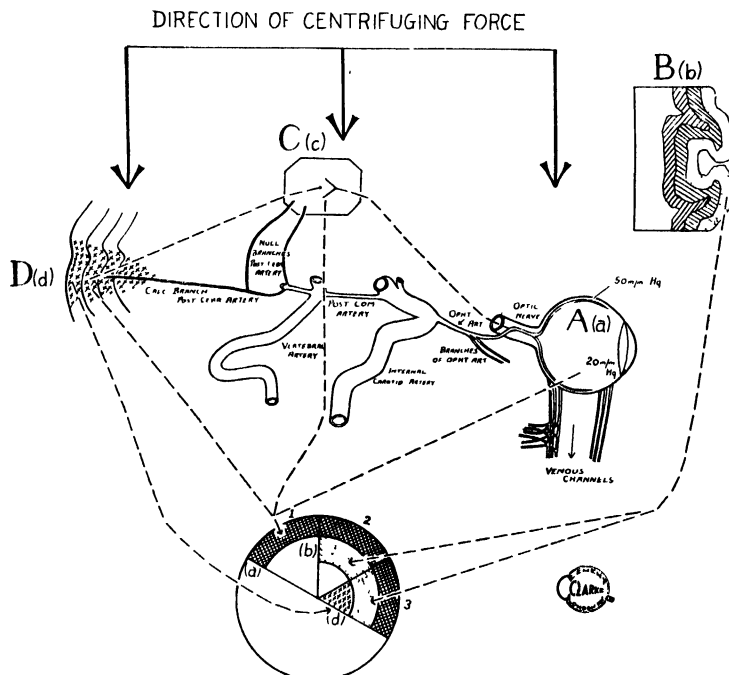


FIG. 10 Schema covering the associated regions affected, which, according to the relative involvement of each, produce the visual and psychovisual phenomena of 'black-out'

- | | |
|---------|---|
| | <p>A, The eye with its end-artery blood supply</p> <p>B, Cortical area representing conscious mental processes and initiating effector responses</p> <p>C, The area of lower visual centres, external geniculate body, pulvinar and upper quadrigeminal body, supplied by end-arteries, fulfilling the duty of intermediate relay stations</p> <p>D, Corticovisual area</p> |
| Areas | <p>a, Visual simple 'black-out' produced through mild action at the three points (a), (c), and (d)</p> <p>b, 'Black-out' with loss of power of thought or emotional states produced by more pronounced action upon (a), (b), (c), and (d)</p> <p>c, 'Black-out' from profound effects upon (a), (b), (c), and (d), with emphasis on the psychovisual cortex (d), embodied in dream states, etc. Beyond this condition lie fainting and collapse</p> |
| Effects | <p>1, 2, and 3 show the stages reached in diagrammatic form</p> |

strain was the first impression, derived from the terrific impact of the aircraft against the resistance of the air at the point of turn. A sense of numbness of the facial skin is experienced with a feeling of weakness in the limbs. Visual disturbances which may range from a mere haziness to a complete blackness next occur, lasting from 1 to 20 seconds, after which, unless in exceptional cases, recovery is instantaneous. After-effects are unusual, but may include severe fainting, dreams, and hallucinations. The cause of this syndrome is considered to be the centrifugation of

the blood supply from the brain, and perhaps retardation of the blood-flow in the ophthalmic arteries. Two methods of combating 'black-out' are suggested: (i) postural, which necessitates bending the body sharply forward so that the thigh angle is narrowed; and (ii) mechanical, in which adjustable seats and body belts are provided. The use of oxygen as a preventive does not seem effective, but carbon dioxide has been found beneficial, possibly as a stimulant to the adrenal secretion with subsequent rise in the systolic pressure.

Livingston, P. C. (1939) *Brit. J. Surg.*, **26**, 749.

Examination of Special Senses

Visual Requirements for Night-Flying

The visual requirements for night-flying include an ability to look from the bright cockpit to distant objects poorly illuminated, and back again. This requires a change in ocular adjustment for intensity of light and the distance of the object seen. C. E. Ferree and G. Rand described a new improved instrument which has been designed for the examination of subjects whose vision must meet such requirements. The multiple-exposure electrical tachistoscope renders possible exact testing of the motor and sensory functions of the eyes, testing of the dynamic speed of vision with either the oculomotor or the accommodative factor emphasized, and the length of time required to change from near to far objects, or the reverse, in combination, or separately. In addition to the special nature of the instrument, the conditions of night-flying are closely simulated by its arrangement in a small enclosure with suitable lighting. Other uses for this instrument were stated to be for general testing of aviators, for age-limiting test, as a means of measuring ocular, oculomotor, and general fatigue, and as an aid to training for greater accommodative facility. The instrument comprises a timing mechanism and 3 electro-magnetically operated shutters.

Ferree, C. E., and Rand, G. (1939) *Amer. J. Ophthalm.*, **22**, 655.

Diseases Associated with Aviation

H. E. Whittingham divided diseases associated with aviation into two groups those, such as yellow-fever, which are imported by aircraft and can be prevented by the sanitary control of aerodromes and aircraft, and those peculiar to persons who fly. Eye affections due to flying include glare, ocular fatigue, and blacking-out. Glare can be overcome by suitable goggles, and ocular fatigue can be helped by means of a weak plus lens and by placing the instruments most frequently looked at in the line of vision. Blacking-out is caused by centrifugal force sending the blood from the head towards the direction of the feet, thus emptying the central artery. The condition can be aided by shouting loudly to contract the abdominal muscle and thus force the blood upwards or by using an adjustable seat which will throw the flyer into a crouching position with the same effect. Noise in aeroplanes can be overcome largely by the use of sound-proof cabins. If vertigo is induced by long steep ascents or descents the airman should swallow often to clear the Eustachian tubes. Anoxaemia occurs at high altitudes, when oxygen must be provided. A low-carbohydrate diet decreases the susceptibility to ballooning of the intestine at high altitudes. Sufficient water should always be carried on long flights. All measures to alleviate fatigue should be undertaken. Air sickness is probably of vago-sympathetic origin and about 80 per cent of susceptible persons can overcome it by repeated flights. Sedatives may be taken before the flight and are of special use in nervous subjects. In warm climates sun-proof blinds must be provided to protect the flyer from the sun.

Whittingham, H. E. (1939) *Proc. R. Soc. Med.*, **32**, 455.

BACKACHE AND LUMBAGO

See also Vol. II, p. 251.

Aetiology

Postural and Occupational Factors

In correct posture, as defined by A. Wesson, a plumb-line held against a normal human being should pass through the mastoid process, cervical spine, lumbar spine,

hip-joint, knee-joint, and ankle-joint. In this position the anterior and posterior muscles of the body have the minimal amount of work to do to keep the body upright. Deviation from the normal results in increased curves in the spine with a corresponding alteration in length of the muscle-fibres leading to an imbalance in their power. Some groups of muscles are shortened and hypertrophied and others lengthened and weakened. This makes them peculiarly liable to sudden strain resulting in 'rheumatic' pains. Alteration in the position of the spine leads to changes in the lateral abdominal muscles and the abductors and adductors of the opposite limb; this in turn leads to standing on one leg and tilting of the pelvis. Low-back and sciatic pain is often found in drivers of heavy motor vehicles and labourers who have to lift heavy weights in a stooping position. Wesson considers this to be due to the flexing of the hips and knees for long periods causing the hamstrings to contract and the glutei to stretch. The shortened hamstrings then pull on and flatten the lumbar spine which loses much of its mobility. In such a condition sudden extension of the hip-joint, plus any excessive load, as in applying a foot-brake suddenly, leads to acute strain on the hamstrings, and secondary strain on the sacro-iliac joint and its muscles. This results in pain in the buttocks, and, later, typical sciatic pain.

Wesson, A. (1938) *J. R. Inst. publ. Hlth*, 1, 733.

Treatment

Injection of Novocain

Arthritis of articulations is the principal cause of ischialgia, especially of the joint between the last lumbar vertebra and the os sacrum. It results from malposition of the surface of bones in small joints, produced by malformation in the condyloid processes or vertebral bodies, or by diminution of the intervertebral fibrocartilage, or by an infective or toxic agent. Patients with ischialgia were treated by S. Teneff with injections into the affected joint at the level of the 5th lumbar vertebra, 2 to 3 cm. lateral to the linea interspinosa on the affected side. The point of the needle touched the surface of the articular processes and of the transverse processes. 20 to 40 c.cm. of a 1 or 2 per cent procaine hydrochloride (novocain) solution was injected. Pain was relieved immediately after the first injection. Most patients received 2 to 5 injections at an interval of one to two days. All the patients treated were cured.

Teneff, S. (1939) *Chirurg*, 11, 237.

BERI-BERI

See also Vol II, p. 313, and Cumulative Supplement, Key No. 125.

Aetiology

L. M. Loeb and R. S. Greenebaum reported a case of beri-beri which was due to inadequate absorption of vitamin B₁ following herniation of the small bowel through the mesentery, and manifested clinically by profuse vomiting and diarrhoea. Macrocytic anaemia and failure to gain weight on a high calorie diet were other signs of deficient absorption. The beri-beri was first suggested by numbness in the epigastrium, spreading over the lower part of the abdomen to the inner surface of the thighs, and finally involving the lower limbs with ultimate production of complete paralysis of them. At operation the presence of 3 previous anastomoses, gastro-ileostomy, gastro-jejunostomy, and a jejuno-jejunostomy were found. The continuity of the stomach and bowel was returned to normal and the hernia was reduced. The patient died on the eleventh day after operation, and at necropsy histological cardiac and nervous changes confirmed the diagnosis of beri-beri. It was thought that the earlier gastro-intestinal symptoms were due to the presence of a duodenal ulcer, but that, during the last 4 or 5 months of life, the presenting clinical picture was that of a low-grade intestinal obstruction further complicated by the anastomoses.

Loeb, L. M., and Greenebaum, R. S. (1939) *J. Amer. med. Ass.*, 112, 1810.

Clinical Picture

In countries where beri-beri and pellagra are both endemic, cases occur which, in addition to the manifestations of beri-beri, have skin lesions resembling those in pellagra or sometimes skin lesions which are not found in this disease, especially a keratosis pilaris-like eruption (phrynodermia). This condition, called by Castellani 'dermo-beri-beri' or 'pellagroid beri-beri', is probably due to deficiency of vitamins A, B₁, and B₂. The signs of beri-beri, such as absent knee-jerks, are present with chronic roughening and pigmentation of the skin of the exposed parts of the body, and also sometimes of the unexposed parts. A keratosis pilaris-like eruption of the type found in avitaminosis, due to deficiency of vitamin A, with numerous horny papules giving the feeling of a nutmeg-grater appears on the extensor parts of the legs, thighs, and arms, and sometimes stomatitis, which may involve the angles of the mouth, occurs. The prognosis is good if diet rich in vitamins A, B₁, and B₂ is given early in the disease. Cod-liver oil may be applied to the keratosis pilaris-like eruption

Castellani, A. (1938) *J. trop. Med. (Hyg.)*, **41**, 294.

BILHARZIASIS

See also Vol. II, p. 323

Treatment

Prevention

F. G. Cawston showed that in India man may be relatively free from bilharzia infection, although it is common in animals. Nasal granuloma due to schistosomiasis is so far unknown in man, but occurs in cattle. Insufficiently watered stock is liable to worm infestations of all kinds, and it is important that infected animals should be either fully treated or destroyed as incomplete treatment results in the parasites leaving their usual site and lying in the liver or migrating to some other place where continued treatment is needed for cure. The local condition in the nose may respond to antimony ointment, but adequate treatment of the general condition is essential. In man anthiomaline, tartar emetic, emetine, antimosan, fouadin, and the *Dn* Belgian compounds have been used with apparent success.

Cawston, F. G. (1938) *J. trop. Med. (Hyg.)*, **41**, 293.

Asthma accompanying Bilharziasis

F. Mainzer discussed a type of allergic bronchial asthma which accompanies bilharziasis. This must be distinguished from pulmonary bilharziasis which arises as a result of bilharzial infection of the intestines or bladder. Pulmonary lesions are common and persist long after the asthma has responded to treatment, so that it becomes obvious that the bronchial asthma was not induced by anatomical changes. Three case reports are given of bilharziasis associated with asthmatic attacks of considerable severity. In each case injections of antimony relieved the asthma, and reduced the liver and spleen to normal proportions. The outstanding features of bilharzial asthma may be summarized as leucocytosis and high eosinophilia, focal infiltration of the lungs with increased striations, and a permanent pyrexia. In addition, a positive intradermal reaction for bilharziasis is given

Mainzer, F. (1939) *J. Allergy*, **10**, 349.

BIRTH PALSIES

See also Vol. II, p. 339.

Peripheral Birth Palsies

J. E. Morison reviewed 29 cases of peripheral brachial paralysis in infants and children including 3 post-natal traumatic lesions. The constant factor in their aetiology was some external interference at birth such as the application of forceps. The clinical picture varied, but most of the cases were consistent with rupture of the nerve roots consequent on overstretching. The cases were treated by splinting,

movement, and massage, and in one case by massage alone. Morison stressed the importance of voluntary movement and the prevention of contraction in this condition. With proper treatment the prognosis is fairly good. Nearly one-third of this series made a complete recovery within 3 months.

Morison, J. E. (1938) *Arch. Dis. Childh.*, **13**, 310.

BITES AND STINGS

See also Vol. II, p. 343.

Arthropoda

Ticks

G. A. Mail and J. D. Gregson of the Dominion Entomological Branch Laboratory, Kamloops, British Columbia, where there are records of 150 cases of human tick paralysis, some of them fatal, point out that, although *Dermacentor andersoni* is as yet the only tick associated with paralysis in North America, at least eight other species of ticks have in other parts of the world been incriminated. The disease is not infrequent in sheep and cattle and is less rare in children than in human adults, perhaps because adults find and remove the ticks more readily. There is not any proof of bacterial or virus infection, and it has been suggested that the tick pours into the host a thermolabile toxin, derived from the salivary glands or from the ova; this view receives some support from the rapid recovery which usually follows removal of the tick. The onset occurs in perfect health with numbness in the lower extremities, without pain or fever, followed by paralysis. From the onset to complete paralysis or even death 3 to 5 days usually elapse.

Scorpions

O. de Magalhães (1938) investigated the poison of the scorpion. The poison has only a single outlet, the aculeus. It is a nervous-system toxin and is not instantaneous in its action, 5 or 6 minutes elapsing between inoculation and the onset of symptoms when a minimal lethal dose is given to an animal. The scorpions of Brazil inject on an average 0.000131 gram each time. The toxicity is greater in the spring and autumn. The central nervous condition is an acute syringobulbia and the respiratory disturbances are probably due to a lesion of the bulbar respiratory centre. Glycosuria has been found after recovery from the poison and gangrene at the site of the sting may be a complication. After the scorpion has stung, the leaves of *Dahlia variabilis* may be placed on the spot because they contain a substance which neutralizes the poison, or the crushed body of the scorpion in alcohol or the viscera of the arthropod, crushed or not, may be applied. The treatment of choice is specific serum therapy which gives a remarkably low death-rate, in one series only 1.81 per cent, as against an alleged figure of 42 per cent without serum.

According to O. de Magalhães (1939): (i) the manifestations of poisoning from the stings of scorpions in animals are confined to the nervous system, (ii) the venom acts principally on the nervous centres, and (iii) the animal is immune against the venom of the scorpion only when its central nervous system is immune. The venom acts on the sympathetic system; peristalsis is increased and abortion may occur. Respiration is disturbed and paralysis of the respiratory centre may be fatal. Tachycardia and arrhythmia are due to the action of the poison on the medullary centres. Scorpion venom also exerts effects on the blood, producing agglutinins, haemolysins, and leucocytolysins and on the endothelium producing haemorrhagins; it has a proteolytic action on the tissues and directly affects smooth and striated muscle. The neurotoxin acts upon the somato-sensory apparatus peripherally and centrally in the cerebrum and cerebellum. It also acts upon the neuro-vegetative nuclei in the medulla. Its action on the cerebrum is shown by convulsions and disturbances of speech. Typical cerebellar syndromes were obtained in laboratory animals. The syringobulbar symptoms must be diagnosed from those due to tumours and haemorrhage and, with greater difficulty, from true cavitary gliomatosis.

Magalhães, O. de (1938) *J. trop. Med. (Hyg.)*, **41**, 393.

— (1939) *ibid.*, **42**, 1.

Mail, G. A., and Gregson, J. D. (1938) *Canad. med. Ass. J.*, **39**, 532.

Snake-Bite*Treatment*

C. H. Kellaway, discussing snake-bite in Australia, stated that only 2 antivenenes are available and that the univalent tiger-snake antivenene is generally applicable, but is useless against the bites of the brown snake and death adder. Univalent tiger-snake antivenene, if of high titre, is moderately effective against several other venoms. An antivenene, 10 c.cm. of which neutralizes 3.3 mg. of dry tiger-snake venom, neutralizes 2.4 mg. of black tiger-snake venom and about 1 mg. of copperhead or taipan venom. After the bite of a large tiger snake from 60 to 100 c.cm. of high titre antivenene should be given intravenously. Sensitiveness to horse-serum protein should be tested. This may be done by giving intradermally 0.1 c.cm. of a 1 in 10 dilution of horse serum. If no skin reaction occurs, the treatment may proceed at once. If, however, the patient is sensitive to horse-serum protein, desensitization should be effected rapidly.

M. H. Finlayson and J. M. Grobler describe the method of preparing a dry stable provisional standard serum for cobra antivenene. The Provisional Standard Unit is the specific neutralizing activity for cobra venom contained in 0.325 c.cm. of the Provisional Standard Serum. It is suggested that this unit should be provisionally adopted in S. Africa. The dried serum was found to be extremely stable when tested over a period of 12 months and stored in the refrigerator at -2° to -4° C. The Provisional Standard Serum was found to retain its potency when the dried serum was dissolved in 60 per cent glycerin. The potency of cobra antivenenes has been successfully determined in terms of the Provisional Unit, and many variations were shown between different commercial antivenene preparations which are marketed in S. Africa.

Finlayson, M. H., and Grobler, J. M. (1939) *S. Afr. med. J.*, **13**, 9.
Kellaway, C. H. (1938) *Med. J. Aust.*, **2**, 585.

BLACKWATER FEVER

See also Vol. II, p. 361, and Cumulative Supplement, Key No. 135.

Treatment

F. Clair discussed the treatment and prevention of blackwater fever. In the Sudan, haemoglobinuria occurs in November and December and usually attacks subjects who have lived in the region a year or two and who have previously suffered from malaria. An acute myocarditis sometimes develops and the first heart sound is scarcely audible. Oliguria and pathological blood-changes close the picture. In the author's experience surgical intervention is very dangerous in malarial subjects. Prevention should be practised when possible by rest in bed, lacto-vegetarian diet, calcium chloride, and diuretics. The bowels should be kept open, and the patient should periodically be gently massaged. In the treatment of the condition, oxygen therapy by subcutaneous injection (care being taken not to pierce veins or venules) should be practised. Troop-ships, expeditions, and military contingents in the tropics should be provided with the necessary equipment.

Clair, F. (1939) *Monde méd.*, **49**, 655.

BLADDER DISEASES

See also Vol. II, p. 374, and p. 34 of this volume.

Carcinoma*Treatment*

X-irradiation—Successful X-ray treatment of cancer of the bladder was carried out by S. C. Levine *et al.*, using the Chaoul contact technique. The bladder was first marsupialized. An endotherm excision of the bulk of the cancer was undertaken when possible, an opening into the bladder maintained so that the low-voltage tube might be inserted. This apparatus was limited to a voltage range of 50 to 60 kv. with a

filtration of 0.2 mm. of copper and 4 or 5 days were allowed to elapse in order to obtain definite anchoring of the bladder to the abdominal wall. An hour before commencing X-ray treatment an injection of morphine sulphate was given, and, until the wound was well healed, rectal injections of evipan sodium or avertin were also used. A suitable cone was chosen to cover the entire growth, and placed *in situ*. The tube was then attached to the cone so that the anode end of the cone was slipped into the open end of the cone. Target skin distance was 3 or 5 cm. A dose of 2,500 *r* was given on alternate days. A series of 9 or 10 treatments, spread over 18 to 20 days, giving a total dosage of 22,500 to 25,000 *r* was found to give satisfactory regression. After a suitable interval allowed for palpation of the bladder wall, the wound was closed. In a case report quoted, no evidence of the tumour could be found two months after the second operation, and the patient appeared free from symptoms.

Levine, S. C., Pack, G. T., and Gallo, J. S. (1939) *J. Amer. med. Ass.*, **112**, 1314

Stone

Prognosis

E. W. Hayward and B. L. Mehta analysed 224 operations for vesical calculus in India, treated by suprapubic lithotomy by the open method (93), by the closed method (59), or by litholapaxy (72). It did not appear to affect the mortality whether the closed or open method was used. No relation was observed between the chemical composition of the stones and the death-rate. As regards seasonal mortality, all the cases which proved fatal without a fully ascertained cause occurred in the hotter months, and the observations made were in agreement with the rule that the higher the blood urea the greater the operative risk. The chief factors influencing the mortality of vesical calculus operations were the general condition of the patient, his age, his blood urea and, to some extent, the climate.

Hayward, E. W., and Mehta, B. L. (1938) *Indian med. Gaz.*, **73**, 659

Cystitis

Treatment

Sulphanilamide.—After careful investigation D. R. Mitchell *et al.* have arrived at a method of administering sulphanilamide in cases of cystitis and pyelitis which produces the minimal toxic effects. By this minimal effective step-dosage regimen, the patient is first given a 5-grain dose of sulphanilamide. If no adverse reactions are noted, 5 grains are given 3 times a day after meals for the first day, 10 grains 3 times a day are given for the second day, and 15 grains 3 times a day for the third. If necessary, dosage is increased 15 grains per day until a dosage of 75 grains is being given. The first clear specimen of urine voided is taken as an indication that the dosage is adequate. In nearly all cases a sterile urine is produced in 2 to 4 days, provided no complication is present. If no improvement is obtained by the time the daily dose has reached 60 grains, it is not considered that benefit will result from further treatment. The maximal necessary dose of the drug is continued for 3 more days after the effective urinary concentration has been reached, and to prevent relapse the drug is withdrawn gradually by 5 grains per day. When a daily dosage of 10 grains is reached, this is continued for 7 to 10 days. Sulphanilamide is considered the drug of choice in the treatment of cystitis and pyelitis, particularly in the pyelitis of pregnancy. The organisms which respond most readily are *Bact. coli*, *B. proteus*, and staphylococci. Faecal streptococci are completely resistant.

Benzochrome compared with other antiseptics.—A. Decker and M. Texon, after reviewing the action of various urinary antiseptics, reported the results of a clinical study of the use of benzochrome for this purpose. Oil of sandalwood, once thought to be specific for gonococcal urethritis, was found to be germicidal to staphylococci, but to have no influence on *Bact. coli*. Hexamine requires acid concentrated urine for its action. Dyes, such as methylene blue and acriflavine in an alkaline medium, are fairly efficient. Pyridium and azo-dyes act equally well in acid or alkaline medium, no special diet being required for their use. They soothe inflamed mucous membranes, and retard the action of certain *coli* and staphylococcal organisms. Hexylresorcinol, although of little use in the treatment of urinary infection in children, is of value in adults with chronic infection due to the staphylococcus and *B. pyocyaneus*. The ketogenic diet often produces gastro-intestinal upsets, and ammonium mandelate is probably better for producing the acid urine on which the success of this treatment depends. Sulphanilamide has been found to have definite

bactericidal power against such organisms as the gonococcus and *Aerobacter aerogenes* when they are present in the urine. The authors treated 25 consecutive patients suffering from such conditions as cystitis, pyelitis, pyelocystitis, pyelonephritis, kidney abscess, and nephrolithiasis with the azo-dye compound known as benzochrome. No special diet was given and no attempt was made to change the reaction of the urine. All the urines examined were acid. The symptoms were relieved, particularly scalding on micturition; in most cases the urinary abnormalities disappeared, though in a few pyuria persisted in spite of the relief of symptoms.

Decker, A., and Texon, M. (1938) *Amer. J. Surg.*, **41**, 449.

Mitchell, D. R., Greey, P. H., and Lucas, C. C. (1939) *Canad. med. Ass. J.*, **40**, 336.

Tuberculosis

Prognosis

Two possible end-results of tuberculous cystitis are illustrated by 2 cases of J. B. Wear. In the first case the ureter of the unaffected kidney became obstructed. The patient was treated with nephrostomy on that side and nephrectomy on the other with favourable results. In the second case the bladder became functionless as the result of sclerosis and destruction by fibrous tissue. The left ureter was transplanted into the sigmoid colon and 5½ years later the patient was in excellent general condition and was opening his bowels every 4 hours. Excretory urograms showed the ureter and calyces to be dilated to twice their normal size.

Wear, J. B. (1938) *Arch. Surg., Chicago*, **37**, 821.

BLINDNESS

See also Vol. II, p 407, and p 128 of this volume.

Tabetic Optic Atrophy

Treatment

J. E. Moore *et al.* discussed the treatment of primary optic atrophy due to syphilis. They studied 191 cases, 65 of which received no treatment, 28 received inadequate routine antisyphilitic treatment, 34 received an adequate similar treatment, 28 were treated with subdural, intraspinal, or intracisternal injections of arsphenaminized serum plus routine treatment, 9 were treated by malaria therapy, and 27 received combinations of 2 or more of these treatments. They found that in untreated cases blindness occurred in 32 per cent within one year, in over 50 per cent within 2 years, in more than 75 per cent within 4 years, and all with very rare exceptions were blind by the seventh year. They found that inadequate routine treatment had no effect on the optic atrophy, but that adequate treatment retarded the process and that only 69 per cent of such patients were blind by the ninth year. Subdural injections arrested the condition in about half the patients so treated, but here there is danger of inducing sudden complete blindness in about 10 per cent of cases. In those treated with malaria about 85 per cent showed arrest of the atrophy, though the balance succumbed to blindness within 3 years. Moore *et al.* found that untreated optic atrophy always becomes bilateral and eventually leads to blindness in most cases, but if treatment was begun when the condition was unilateral, it did not become bilateral in 70 per cent of this series.

Moore, J. E., Woods, A. C., Hopkins, H. H., and Sloan, L. L. (1938) *J. Amer. med. Ass.*, **111**, 385.

Toxic Amblyopia

Treatment

Vitamin B—Because toxic amblyopia sometimes accompanies vitamin B deficiency, L. V. Johnson treated amblyopia due to tobacco and alcohol with thiamin chloride (vitamin B₁). Five patients were treated with 12 mg. of thiamin chloride daily and, when the disease was unaccompanied by optic atrophy and the treatment was accompanied by cessation of alcohol and tobacco intake, good results were obtained; 60 mg. of nicotinic acid was given in addition to 2 of the cases, a number which was too small to assess the results of the treatment.

Johnson, L. V. (1939) *Arch. Ophthalm., N.Y.*, **31**, 602.

Night-Blindness*Treatment*

Vitamin A.—According to C. Vaillant and L. Gillis a high proportion of poorer children suffered from night-blindness, and, in the general community, such impaired vision may be responsible for motor accidents in the dark. In moderate cases the period of accommodation of the eye to sudden changes from light to darkness took 30 seconds, and in severe cases the vision in the dark was never adequate. A biophotometer was used to measure the deficiency, and the interval between the appearance of the quincunx (the disposition of 5 objects, 4 at the corners and 1 in the centre of a square or rectangle) of 5 illuminated spots and the disappearance of the central spot was adopted as the method of measuring the adaptation rate (normal time 31 seconds). The case of a girl, aged 20, in whom this reaction took 85 seconds and whose night-blindness was severe was reported, and the eyes ached when exposed to bright light; daily oral administration of 10,000 international units of vitamin A (essogen) for a fortnight reduced the interval to 60 seconds, though then there was not any improvement in other respects, but after the dosage was increased to 15,000 units daily for the next 2 weeks, the adaptation rate shortened to 22 seconds, vision in the dark being much better. A daily maintenance dose of 5,000 units of essogen has been continued for 2½ months and has obviated any disability and cause of complaint.

Vaillant, C., and Gillis, L. (1939) *Lancet*, 1, 149.

BLOOD EXAMINATION

See also Vol. II, p. 457; Cumulative Supplement, Key Nos. 163–169, and pp. 21 and 52 of this volume.

Cellular Changes*Methylene-Blue Reaction*

C. H. Smith has shown that, if the blood of a healthy infant was mixed with a dilute solution of methylene blue in sodium citrate and exposed to the cold, the dye was rapidly removed by adsorption on to the red blood-cells. This reaction was most active during the first 4 months of life. It was found that the rate of adsorption depended upon the time the dye was in contact with the red cells, and rapid sedimentation therefore reduced adsorption. Consequently the minimum decolorization occurred during acute illness but returned in the convalescent stage. The capacity of the red cells to adsorb depends on the presence of serum or plasma. The dye was adsorbed into the stroma of the cells and was rapidly liberated in warm temperatures. Clinically it was found that marked decolorization occurred in nutritional anaemia.

Smith, C. H. (1939) *Amer. J. Dis. Child.*, 57, 1223.

Coagulation*Measurement of Clot-Retraction*

R. G. Macfarlane described a method of measuring clot-retraction. The apparatus included a graduated centrifuge tube with the scale marked in 0.1 c.cm. divisions, a glass rod which is half an inch longer than the tube and has a 'button' expansion near one end, and a cork to fit the mouth of the tube. More than 5 c.cm. of blood is taken from a vein in the arm and is run into the centrifuge tube. The glass rod is put into the tube and the cork is fitted. The tube is placed in a warm bath at 37° C. and examined for coagulation of the contained blood. An hour after firm clotting, it is removed from the bath. If retraction has taken place, the clot has shrunk away from the walls and is attached to the rod only. By sliding the rod through the cork, the clot, supported on the expansion, can be raised clear of the expressed fluid and the volume of the latter measured. Retraction is estimated as a percentage of the original volume of blood; if 5 c.cm. of blood after clotting express 3 c.cm. of fluid, the retraction is $\frac{3 \times 100}{5}$, namely 60 per cent. It was found that the most suitable time for taking a single reading was one hour, since a delay in retraction could be demonstrated. Blood was taken from 50 patients whose ages varied from 16 to 48 and retraction was measured in each case. The results range from 48 to 64 per cent with a mean of 55 per cent. Factors influencing retraction are as follows: (i) a rise

in temperature increases the rate up to 47° C. after which it is inhibited; (ii) it is diminished by a reduction in the number of platelets below the figure of 100,000 per c.mm.; (iii) as measured in a large series of pathological cases, it was much reduced in jaundice, lobar pneumonia, and thrombopenia. The impaired retraction

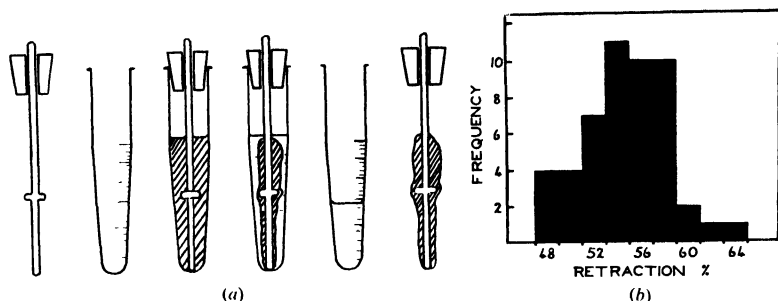


FIG 11 — (a) Diagram showing glass rod, cork, and graduated centrifuge tube, and method of removing clot to measure serum expressed (b) Histogram showing frequency distribution of retraction readings from 50 normal persons (From *The Lancet*, 1939)

did not depend on the depth of the jaundice, the highest van den Bergh reaction being obtained when this was normal. Apart from thrombopenic purpura, other haemorrhagic states are not associated with any alteration in the retraction rate.

Macfarlane, R. G (1939) *Lancet*, 1, 1199.

Serological Tests

Formol-gel and Takata-Ara Reactions

A. Hassan and M. Salah studied the formol-gel and the Takata-Ara reaction in 600 sera. The formol-gel test depends on the formation of a gel and opacity in serum to which a drop of formalin is added. The Takata-Ara reaction depends on the formation of a sediment and opacity in serum in a wide range of dilutions when mercuric chloride and sodium bicarbonate are added. In 85 per cent of the sera there was a similarity in the results of the two tests. The formol-gel test was found to depend upon a hyperglobulinaemia of 4 per cent. The degree of gellation to the hyperglobulinaemia was more valuable than the opacity and the results were not quantitative. The Takata-Ara test, if positive, indicated a relative increase in the serum globulin or a marked decrease in the serum albumin.

Hassan, A., and Salah, M. (1939) *J. trop. Med. (Hyg.)*, 42, 169.

Physical and Chemical Changes

Oxygen Saturation

A. Keys pointed out that the most obvious criterion for estimating the adequacy or deficiency of the circulation was the difference in the oxygen content of the arterial and venous blood. Normally the arterial saturation is always between 93 and 98 per cent. Experiments were conducted on 59 normal men and 24 normal women, between the ages of 18 and 50, to ascertain the values of the frequency range for the oxygen saturation of blood from the veins of the arm and leg of the subject at basal rest and under the influence of some deviations from basal rest. It was found that the oxygen saturation of blood in the veins of both arms and legs displayed considerable variation, even when external and physiological conditions were maintained as constant as possible; this variability is in sharp contrast with the findings of other authors. The average venous saturation shown was 68.2 per cent, and a range of 25 to 85 per cent in contrast to what is often stated to be the 'normal limit', namely 60 to 85 per cent. The percentage oxygen saturation of the blood from the vein of the arm in normal women tends to be slightly lower and the oxygen yielded to the tissues, per 100 c.cm. of blood, tends to be slightly greater than in normal men in the basal state.

Keys, A. (1938) *Amer. J. Physiol.*, 124, 13.

Chemical Analysis

The possibility of some correlation between the chemical composition of blood obtained at necropsy and structural renal changes found at necropsy prompted R. C. Hamilton to make a study of a series of chemical analyses of blood obtained from 104 cadavers. Serum was used because of the presence of clots in post-mortem blood, but the concentrations of sugar, non-protein nitrogen, and creatinine are essentially the same as in whole blood. The chlorides, however, are higher in serum. Determination of blood sugar after necropsy showed extreme results of questionable value; neither non-protein nitrogen nor chlorides yielded information of any definite value, but the remarkable stability of creatinine rendered it useful in these studies. It was found that the creatinine content of cadaveric blood gave no indication of renal damage which may have been present, and further that such creatinine determination cannot be regarded as an index of renal function during life. It is mentioned that Myers and Lough showed that a rise in blood creatinine was a most important sign of loss of renal function, but in the studies under consideration, high creatinine determinations were in several cases quite unrelated to renal damage.

Serum Phosphatase Test

J. M. Looney discussed methods of determining serum phosphatase, and recommended wider use of this test for diagnostic purposes, and in the pasteurization of milk. The results are generally expressed according to the methods of Bodansky which calculates as a unit the amount of phosphatase in 100 c cm. of serum which will liberate 1 mg. of phosphorus from sodium β -glycerophosphate at a pH of 8.9 in one hour at 37° C. when not more than 10 per cent of the substrate has been used up. Bodansky's method was to incubate 1 c cm. of serum with 10 c cm. of a solution containing 0.5 per cent of sodium β -glycerophosphate and 0.42 per cent of mono-sodium diethylbarbiturate at 37° C. for one hour. The mixture is then removed, cooled in iced water, and 9 c cm. of 10 per cent trichloroacetic acid added. The precipitated proteins are filtered off and the total inorganic phosphorus is determined in 5 c cm. of the filtrate or in an aliquot made up to 5 c cm. with water by adding 4 c cm. of 1.87 per cent sodium molybdate in 10 N sulphuric acid and 1 c cm. of fresh 0.3 per cent stannous chloride. The resulting blue solution is compared in a colorimeter with a potassium acid phosphate solution containing 0.02 mg. of phosphorus which has been similarly treated. It is particularly valuable as an aid to diagnosis in various bone conditions. Among these may be mentioned rickets, Paget's disease, and osteitis fibrosa cystica, in all of which phosphatase levels may be increased 10 to 20 times above the normal values. In metastatic carcinoma it may be increased 2 to 5 times. The highest values are obtained with marked bone activity, whether it consists of formation of new bone or destruction of old. Elevation of levels is reported by some observers to occur at the sixth month of pregnancy, the period of marked ossification in the foetus, but this has not been substantiated. It is stated that obstructive jaundice is associated with a high phosphatase and other forms of jaundice with a low value. The detection of improper pasteurization of milk is made possible by this test which is negative if efficient pasteurization has been performed.

Hamilton, R. C. (1938) *Arch. Path.*, **26**, 1135.

Looney, J. M. (1939) *New Engl. J. med.*, **220**, 623.

Sternal Puncture

M. Hynes described his findings from sternal puncture in normal and in diseased conditions. The marrow-picture may be inaccurate if much blood is withdrawn with the specimen and it is then necessary to repeat the puncture. The normal myeloid-erythroblastic ratio in Hynes's series was a mean of 4.25:1. In leukaemia the marrow is very cellular and the primitive white cells are much increased. The percentage of erythroblasts nearly equals that of normoblasts but the number of primitive red cells is less. Sternal puncture is diagnostic in leukaemia and is specially valuable in 'aleukaemic' forms. After treatment of chronic myeloid leukaemia by irradiation of the spleen, both the blood and marrow pictures became more normal, the improvement being most marked in the nucleated red cells. In polycythemia a great increase in erythroblasts occurs in the marrow and in some cases the segmented polymorphonuclears are said to preponderate in this condition. Pernicious anaemia, achrestic anaemia, and other macrocytic anaemias showed a preponderance of megaloblasts and erythroblasts in the marrow.

In acholuric jaundice the marrow may be almost normal and it may contain an excess of normoblasts, erythroblasts, and megaloblasts. The bone marrow in aplastic anaemia showed a variable state in Hynes's series. One case showed extreme hypoplasia, another marked hypoplasia, another moderate hypoplasia, while a fourth showed an active marrow with a normal differential count. Hynes considered sternal puncture inadequate for the diagnosis of aplastic anaemia. In other more obscure conditions, such as myelosclerosis and agranulocytosis, sternal puncture cannot be used for diagnosis and sternal biopsy is much more useful.

Hynes, M. (1939) *Lancet*, **1**, 1373.

BLOOD PRESSURE, HIGH AND LOW

See also Vol. II, p. 503; Cumulative Supplement, Key Nos. 170 and 171; and pp. 19 and 56 of this volume.

High Blood Pressure

Essential Hypertension

Breath-holding test. - Hines and Brown having elaborated the cold pressor test to study the response of the blood pressure in essential hypertension, D. Ayman and A. D. Goldshine employed a breath-holding test as a stimulus to the blood pressure. The test was simpler and was found to give a greater stimulus than the cold pressor test. It was very useful in the diagnosis of early hypertension and both hyper-reactors and hypo-reactors can be determined. With the subject sitting quietly, blood pressure readings were taken every 5 minutes until a basal level was obtained. The time required varied from 20 to 45 minutes and was shorter for the normal than for the hypertensive patient. A basal level was considered to have been reached when after an adequate fall of blood-pressure readings and 20 minutes' rest it was found that 2 or 3 blood-pressure readings repeated every few minutes were within 10 mm. of each other. Then the patient compressed his nostrils, closed his mouth, and held his breath for 20 seconds, at the end of which the systolic blood pressure was again taken. After the blood pressure had returned to its basal level, the test was repeated and the diastolic blood pressure determined. Six hundred and fifty tests were carried out on 150 subjects, 95 of whom had essential hypertension and 55 of whom had normal blood pressures (below 145 mm. and 90 mm.). The average rise of the pressure readings in hypertensives who had shown a good basal level was 40/7 systolic and 25/4 diastolic. Those with normal blood pressure could be divided into hyper-reactors with corresponding figures of 32 mm./21 mm. and hypo-reactors 11/6 mm./11/7 mm.

Paroxysmal Hypertensive Attacks

M. Demole and E. Rutishauser described a case of paroxysmal hypertensive attacks, co-existing with hyperglycaemia and attacks of pulmonary oedema, which were attributed to the tuberculous infection of the adrenals as found at necropsy. Inflammatory conditions of the glands of internal secretion can well produce a state of temporary hyperfunction or a rapid liberation of hormones. In this paradoxical case, hyperadrenalism and hypertension were caused by adrenal tuberculosis, a condition usually associated with extreme degrees of hypotension. The authors therefore put the question, why do not early stages of Addison's disease produce temporary or transient hypertension?

Relation to Renal Disease

M. Friedman and L. N. Katz experimented on dogs to investigate the relations between (i) hypertension and renal excretory insufficiency, acute and chronic, resulting from damage to renal tissue produced by injection of trypsin into the renal arteries, and (ii) hypertension and renal ischaemia, produced by application of a Goldblatt clamp to the kidneys of animals which had previously received bilateral injections of trypsin and which were consequently suffering from chronic renal excretory insufficiency; in addition, the effect of renal ischaemia of one kidney when the other kidney was simultaneously damaged by trypsin was studied. After trypsin damage there was a temporary post-operative hypertension, but a few days later the blood pressure returned to normal and remained normal as long as 3 months. In the presence of unilateral renal ischaemia produced by the Goldblatt clamp, either applied in animals which had previously received bilateral injections of

trypsin or applied to one renal artery simultaneously with trypsin injection into the other renal artery, hypertension developed; in both cases the blood pressure fell to normal when the ischaemic kidney was removed. These results indicated that renal excretory insufficiency does not cause hypertension, and that hypertension occurred only when there was renal ischaemia or active damage to the renal parenchyma.

Because renal lesions and hypertension so often occur together, many attempts have been made to produce a renal lesion which resulted in hypertension. Experimentally produced ischaemia of the kidney fulfilled these conditions. J. C. Fasciolo, B. A. Houssay, and A. C. Taquini demonstrated that the ischaemic kidney secretes a vasoconstrictor substance which causes a permanent hypertension, and which is active in the absence of the adrenals or thyroid. The presence of healthy renal tissue was shown to eliminate or destroy in varying degree the vaso-constrictor substance.

Ayman, D., and Goldshine, A. D. (1939) *Arch. intern. Med.*, **63**, 899.

Demole, M., and Rutishauser, E. (1939) *Pr. méd.*, **47**, 747.

Fasciolo, J. C., Houssay, B. A., and Taquini, A. C. (1938) *J. Physiol.*, **94**, 281.

Friedman, M., and Katz, L. N. (1938) *J. exp. Med.*, **68**, 485.

High Blood Pressure in General

Aetiology

D. E. Engle and M. W. Binger investigated the blood-pressure response of hypertensive patients to the subcutaneous administration of acetyl- β -methylcholine. They stated that arterial hypertension is due to increased peripheral vascular tone and, since the peripheral vessels are normally exposed to varying concentrations of a vasodilator substance acetylcholine, they observed the effect of a choline derivative on the blood pressure of both normal and hypertensive patients. A slight lowering of blood pressure was produced in normal subjects by 2.5 mg. of acetyl- β -methylcholine. In 33 patients suffering from hypertension due to various causes, the drug also produced a lowering of blood pressure. The percentage decrease of the blood pressure in this group was greater than in the normal. It was therefore presumed that the concentration of acetylcholine at the nerve-endings of the cholinergic vasodilator nerves was subnormal in the hypertensive group and that the peripheral blood vessels were therefore kept in a state of increased tone in this condition. Administration of acetyl- β -methylcholine also reduced the reflex vasoconstrictor response of hypertensive patients to the cold test.

Test of Effect of Smoking

E. A. Hines and G. M. Roth described a standard smoking test for the effect of smoking on the blood pressure. After lying down for half an hour in a quiet room the subject smokes two cigarettes of a standard brand, and, during the smoking and for a few minutes after, the blood pressure and pulse-rate are watched. In order to determine the part played by mechanical and emotional factors in any rise of blood-pressure, a control (the 'cold') test was employed, in which the same procedure was gone through, except that an unlighted cigarette was puffed. The subjects of the test included 30 with normal blood pressure, 20 who reacted normally and 10 who reacted excessively to the 'cold' test, and 56 hypertensives, 11 of whom were non-smokers. The majority of the subjects showed a rise in blood pressure, the excessive occurring only in those with an inherently hyper-reactive vascular system, as shown by the cold test. The rise of blood pressure, however, is not entirely due to a non-specific stimulus acting on a hyper-reactive vascular system, but is partly due to some vasoconstrictive element in the tobacco smoke. The rise of both systolic and diastolic pressure was much less in the non-smoking hypertensives, it was thought because they did not inhale so much as the hypertensives who smoked.

Treatment

Effect of benzedrine.—W. W. Dyer investigated the pressor effect of benzedrine vapour and large doses of the sulphate taken orally on normal, hypotensive, and hypertensive patients. Twenty rapid inhalations of benzedrine vapour were taken by 28 normal and hypertensive subjects, and the blood pressure was observed at intervals of 5, 10, 15, 30, and 60 minutes. The greatest increase in pressure was 10 mm. Hg observed in 4 patients. The majority did not show any change or only a slight increase or decrease of 5 mm. Benzedrine sulphate was given by mouth in doses of 20 to 30 mg. to 23 hypotensives, normals, and hypertensives. The blood pressure usually

rose according to the dosage, but in some patients the blood pressure dropped. In a group of moderately ill patients a single dose of 10 to 20 mg. was given; with 10 mg. a rise of pressure of 10 mm. was recorded in 2 out of 10 subjects; with 20 mg. there was a rise of 10 to 30 mm. in 10 of the 20 cases. Benzedrine sulphate could be given to hypertensives with safety if the blood pressure was watched, but doses of 30 mg. or more should be given with great caution.

X-irradiation.—A. Delachaux and G. Schneider reported the use of irradiation in arterial hypertension. The carotid sinus was irradiated 3 times weekly during 15 to 20 days with short waves, and 15 of 33 patients improved markedly. Chronic nephritis, asystole, and thyroid disturbances are contra-indications. The method produced extreme well-being in the patients and was carried out in the out-patient department. If the first reaction to the treatment is unfavourable, it is better to cease further sittings. The duration of the exposure to the rays is about 2 or 3 minutes.

Delachaux, A., and Schneider, G. (1939) *Schweiz. med. Wschr.*, **69**, 522

Dyer, W. W. (1939) *Amer. J. med. Sci.*, **197**, 103.

Engle, D. E., and Binger, M. W. (1939) *Proc. Mayo Clin.*, **14**, 341.

Hines, E. A., and Roth, G. M. (1938) *Proc. Mayo Clin.*, **13**, 524.

Orthostatic Hypotension

Treatment

Benzedrine. H. M. Korns and W. L. Randall found that, in treating orthostatic hypotension with parendrine, the pressor effect was greater than that of benzedrine, but the patient failed to experience a sense of vigour and stimulation. On the contrary the drug appeared to act as a soporific. The most successful form of treatment was found to be the administration of benzedrine first thing in the morning, and parendrine 40 mg. every 2 hours for 4 doses during the day. No unpleasant reactions were noted. A case report showed that the average daily dose of benzedrine was 80 to 100 mg. Such dosage rendered the patient comfortable. A complication in the form of paroxysmal hypoglycaemia was discovered, but increase of protein intake (from 75 grams to 120 grams) caused the symptoms to disappear. An endocrine disturbance involving the adrenals, thyroid, parathyroids, and pancreas was suspected as the cause of this patient's condition.

Korns, H. M., and Randall, W. L. (1938) *Ann. intern. Med.*, **12**, 253

BLOOD TRANSFUSION

See also Vol. II, p. 530, and Cumulative Supplement, Key No. 172

Technique of Transfusions

In Small Infants

V. L. Collins described a successful method of giving blood transfusions to small infants, whose weight may only be 4 pounds or, as in one case, only one and a half pounds. The method is of special value in haemorrhages of the newborn, anaemia, and icterus gravis neonatorum. The apparatus consists of an ordinary large hypodermic needle (gauge 18, 24 mm. in length, 1.2 mm. in thickness) shortened to 20 mm. with a stilet projecting 4 mm. beyond the end of the needle. The round tip of the projecting stilet can be introduced into the vein and the larger body of the needle will follow into the lumen, the stilet then being withdrawn. The remainder of the apparatus consists of a three-way stopcock, a Record syringe of 20 to 30 c.cm., a metal adaptor and rubber tubing with a lumen of 4 mm. diameter and apparatus for collecting blood. One piece of rubber tubing, 25 cm. long, runs from stopcock to the adaptor which fits the needle. A second piece, 30 cm. long, connects the stopcock to the vessel containing the citrated blood.

The malleolar vein is generally selected. Having first determined compatibility, citrated blood is collected. Under local anaesthesia a transverse or oblique incision is made across the line of the vein proximal to the internal malleolus. The malleolar vein is mobilized with an aneurysm needle and 2 pieces of catgut are passed beneath it in the customary fashion—a distal one for purposes of traction and a proximal to tie the needle in the vein later on. The vein is cut

half across and the needle and stilet are introduced. The Record syringe is attached to the stopcock, and the rubber tubing is connected to the flask of blood. The tap is adjusted and blood drawn into the syringe; any air in the syringe is expelled through the tube. The stilet is removed as soon as the blood is dropping in this tubing and the adaptor is fitted into the needle in the vein. The blood is then forced into the vein and refilling of the syringe, with adjustment of the stopcock, will furnish the desired amount of blood. With the transfusion completed, the catgut sutures may be removed and a dressing applied. To an infant weighing 6 pounds, it is suggested that 3 fluid ounces of blood should be given in an average time of 20 to 30 minutes. In larger children, the continuous drip method may be more advantageous.

Conserved Blood

F. Corelli described a new and interesting method of transfusion of conserved blood evolved after a few years' experiments. In the course of using sodium thiosulphate to bring about desensitization in allergic individuals, the author observed the anticoagulant effect of this substance; this led him to try it for transfusion purposes. One advantage of the preparation lies in its desensitizing effect. It was found that 7.5 c.cm. of sodium thiosulphate was sufficient to keep 100 c.cm. of blood uncoagulated for over a month. Leucopenia is observed after a few days but the numbers of monocytes and lymphocytes are maintained even after 20 to 30 days. There is a slight haemolysis after 5 to 10 days, which can be disregarded for practical purposes if larger quantities of blood are transfused. Blood taken from individuals in whom the Wassermann and Kahn reactions were negative was stored in a refrigerator at temperatures ranging between 2° and 5° C. and before use was put in a bath at 35° to 38° C. for about 5 minutes, after which transfusions were performed without any reaction. The author's experience was confined to 450 transfusions, only 8 per cent of all cases showed a slight reaction, which manifested itself in transient mild preplexia.

Placental Blood

J. Halbrecht, discussing the use of cadaver or placental blood for transfusion, pointed out the advantage of placental blood over fresh blood in countries where malaria is endemic, inasmuch as malarial organisms do not pass the placental filter and die rapidly in preserved blood. The method is simple and can be carried out in any hospital. At every birth he has obtained an average of 50 to 60 c.cm. (with a maximum of 160 c.cm.) The blood was allowed to flow into the flask from the end of the cord, aspiration being unnecessary. As an anticoagulant, a 3.8 per cent solution of sodium citrate was employed. The slight haemolysis occurring in the first 48 hours was harmless. The blood is kept in a refrigerator at 4° to 5° C. for as long as 14 days. Of the 48 samples cultured 4 were contaminated with *Staphylococcus aureus*. No blood from placentas from cases in which the mother had fever just before or during labour was ever used. Syphilis was excluded in the usual way. As soon as the blood was obtained, its group was determined and the flask labelled accordingly. Before transfusion, each blood was separately cross-tested against the blood of the recipient. This may take time when blood from 5, 6, or more placentas are pooled for a large transfusion. The author has given 116 transfusions of blood obtained from 520 placentas. The transfusions were given to children as well as to adults, the amount given varying from 10 to 15 c.cm. per kg. in infants to 5 to 10 c.cm. in adults. The results obtained are not inferior to those obtained in similar conditions with ordinary fresh blood. In this series there were no serious accidents and only 4 reactions, 3 consisting of a chill and 1 of dyspnoea and tachycardia. This source of blood is urged and the possible throwing away of 50 to 60 c.cm. of blood with each placenta is condemned as a pitiful waste.

A. P. M. Page *et al.* employ as receiver a 300 c.cm. conical flask containing 80 c.cm. of physiological saline made from doubly distilled water; a cotton-wool bung is fitted so that the whole may be autoclaved. To the outside of the flask are strapped (i) a glass ampoule containing 1 gram of recrystallized sodium citrate and (ii) a test-tube to collect blood for a Wassermann reaction. Just before use the sodium citrate is added to the flask. Alternatively 25 c.cm. of the preservative used by the Moscow Institute of Haematology may be added to 100 c.cm. of water before use. A citrate saline may be used as an anticoagulant. When the baby is born the cord is clamped immediately with 2 artery-forceps, without waiting for pulsation to cease, and the infant is separated and handed to an assistant. The distal 6 in. of the cord

is incised with sterile scissors, the cord being controlled by the finger and thumb of the right hand, the left hand controlling the uterus. The assistant holds the collecting receptacle and the operator directs the blood into the flask without allowing any part of the cord to touch it. During a uterine contraction the blood flows freely and in the intervals the cord is pinched by the finger and thumb to prevent spilling. Heating the blood to body temperature before transfusion was unnecessary and

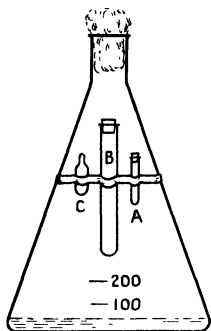


FIG. 12—Receptacle for blood. A—tube for grouping B—tube for Wassermann C—ampoule containing sodium citrate (1.0 g.) (From *The Lancet*, 1939)

perhaps harmful. No difficulties arose in the separation of the empty placenta nor, as measured by repeated blood counts, was there any damage to the quality of the baby's blood. The average yield of blood was 80 c.cm. The authors consider it preferable to ordinary adult blood because it contains no food allergens and because its clotting power is greater, thus rendering it of particular value in dealing with haemorrhage. The authors consider rigid observance of the technique laid down for sterile collection is essential if contamination is to be avoided.

Use of heparin as anticoagulant.—A stable, potent preparation of heparin was used as an anticoagulant by S. W. Sappington in 40 blood transfusions. In 17 of these heparinization was performed *in vitro*, the blood being withdrawn from the donor, heparinized, and injected into the patient; 23 were performed by the *in vivo* method, in which the donor received an injection of heparin prior to withdrawal of the blood, which was immediately transfused. The quantities of blood used in this study were 500 c.cm. in each case. The heparin used was a sterile 5 per cent solution of the drug, containing 500 units per mg.: (the unit is the amount of heparin which will prevent clotting of 1 c.cm. of cat's blood for 24 hours when kept in the cold). When the *in vitro* method was used, 20 to 150 mg. of heparin were added to the blood. All bloods

showed normal coagulation times before transfusion. Results showed that when 50 mg. of heparin was added, the patient's clotting time immediately after completion of transfusion was 73 minutes. Half an hour later it was 50 to 60 minutes and then it gradually dropped to normal. When 150 mg. was used the blood taken 15 and 60 minutes after completion of transfusion remained unclotted for 16 hours. In the second method donors received intravenous injections of heparin of approximately 1 mg. per kg. of body weight, i.e. about 1.5 c.cm. of the 5 per cent solution. In a case in which the clotting time previous to injection was 13 minutes, and 70 mg. of heparin were given, the clotting time one minute after injection was 95 minutes. Ten minutes later, it was 90 minutes, and half an hour after injection 100 minutes. One hour after injection it had dropped to 70 minutes. Larger doses resulted in increased prolongation of fluidity.

The donor's blood was withdrawn 7 or 8 minutes after injection with heparin and given to patients immediately. Except when very large doses of heparin had been administered to donors, no changes in the coagulation time of the patient's blood were observed. No toxic effects were associated with the experiment. It was found more suitable to use a 16 gauge needle as the flow slowed and stopped after the first 350 c.cm. when an 18 gauge was used. An alternative method was suggested by which an 18 gauge needle was used until the flow stopped and then replaced with another similar needle, a second venepuncture being made. Clotting apparently occurred in the small channel of the needle, whereas the same blood remained unclotted in a flask for several days. In the *in vitro* group addition of larger quantities of heparin allowed the satisfactory use of an 18 gauge needle, and in one case, in which 75 mg. of heparin were used, the blood was banked for 48 hours and transfused with a small needle with no difficulty.

Collins, V. L. (1938) *Med. J. Aust.*, 2, 1121.

Corelli, F. (1939) *Klin. Wschr.*, 18, 716.

Halbrecht, J. (1939) *Lancet*, 1, 202.

Page, A. P. M., Seager, K. G., and Ward, E. M. (1939) *Lancet*, 1, 200.

Sappington, S. W. (1939) *J. Amer. med. Ass.*, 113, 22.

BONE DISEASES

See also Vol. II, p. 553.

Arachnodactyly

J. Harrison and M. J. Klainer reported a typical case of arachnodactyly of particular interest because it showed practically all the deformities associated with the syndrome, also demonstrating the familial and hereditary aspects of the disease. Five persons in this family showed varying degrees of arachnodactyly—the patient a girl of 6 years, her mother, the patient's brother (2 years her senior), the patient's uncle, and a cousin (not the child of the affected uncle).

Harrison, J., and Klainer, M. J. (1939) *New Engl. J. Med.*, **220**, 621.

Osteitis Condensans

J. Shafer reported a case of osteitis condensans of the ilium in an athletic man, aged 23 years, who complained of pain and weakness in both lower extremities. This form of osteosclerosis, which was originally described by T. Bársony and F. Polgár, could be diagnosed only by radiological examination, was a benign condition, and did not influence the span of life. Its aetiology was unsatisfactory, but it might follow injury; it was not associated with osteoarthritis of the adjacent sacro-iliac joint. It might be present, as shown radiologically, without any symptoms.

Bársony, T., and Polgár, F. (1928) *Munch. med. Wschr.*, **51**, 365.

Shafer, J. (1938) *Lancet*, **2**, 1229.

Osteitis Deformans*Aetiology*

Ingestion of fluorides in small quantities for a long period of time has been followed by extensive osteosclerosis in man (Bauer, Bishop, and Wolff), and it has been suggested that osteitis deformans should be investigated from this point of view (Sutro). Accordingly W. A. Wolff and J. T. Bauer analysed the cranial bones of six well-defined cases of osteitis deformans and found that the fluorine content was much lower than the average values for normal bones; it therefore follows that chronic fluorine intoxication is not an aetiological factor in osteitis deformans.

Bauer, J. T., Bishop, P. A., and Wolff, W. A. (1937) *Bull. Amer. clin. Lab.*, **3**, 67.

Sutro, C. J. (1935) *Arch. Path.*, **19**, 159.

Wolff, W. A., and Bauer, J. T. (1938) *Bull. Amer. clin. Lab.*, **3**, 209.

Acute Osteomyelitis*Of Superior Maxilla*

N. F. Lacy and L. P. Engel reported a case of acute osteomyelitis of the superior maxilla occurring in an infant 2 weeks old following abscesses in the posterior auricular region and the left bucco-gingival fold. On the tenth day the face was swollen and a fistula appeared below the inner canthus of the left eye. On admission there was purulent discharge from this fistula and from 3 smaller openings in the alveolar ridge. Thick pus was also obtained from the ostium of the antrum. There was swelling of the left side of the face, oedema and redness of the lower lid, and a sero-purulent ocular discharge. The infant's general condition was poor and both the spleen and liver were palpable below the costal margins. Operation was performed and a small antral window was made under the left inferior turbinate. A probe placed in the antrum met probes passed through the fistula on the face and through one of the openings on the alveolar process. Three months after drainage the patient was well, but the sinus on the alveolar process was not completely healed. The authors consider that facial drainage should be avoided if possible, as disfiguring scarring results. Drainage through the mouth, though it destroys some tooth germs and necessitates wearing a dental plate later, followed by drainage through the antrum is preferable. The presence of previous abscesses points to this case being the result of haematogenous infection. The maxilla, rather than the antrum, is regarded by most authorities as being the primary site of infection because the antrum is very small compared with the tooth sockets from which the infection probably comes. Aetiological factors include birth trauma, dental caries, maternal leucorrhoea, infected nipples, and an endogenous infection. In the case

recorded the nipples had been infected. Some observers believe that infection around the tooth buds may be the source of the osteomyelitis. Positive blood cultures have been found in some cases, proving the theory of haematogenous origin. The prognosis in this condition is usually good.

Treatment

The value of conservative treatment in many cases of osteomyelitis was doubted by J. A. Key. Immediate operation was indicated on (i) patients with a mild infection who are not acutely ill; and (ii) severely ill patients with a spreading infection who are in good general condition. The severely ill patient not in a good general condition should be put to bed, his pain relieved by morphine, and the extremity immobilized, preferably with the application of a massive hot wet pack and with traction when practicable. Dextrose should be given intravenously. Toxoids, vaccines, and staphylococcal bacteriophage are not of any value in an acute infection. Conservative treatment should not be continued for more than 12 hours. When adequate rest has been secured, surgical intervention was advised whether or not suppuration was present.

Maggot therapy.—S. Maddock and D. Jensen described the method of treatment and results obtained in 29 cases of haematogenous osteomyelitis treated with maggots. In all cases a preliminary operation of Orr's type was done. One week after the operation in chronic osteomyelitis and 4 weeks after in acute cases, the petroleum gauze was removed and the maggots inserted. Dressings were changed daily to keep the skin in good condition and to remove some of the maggots, if they were crowding and causing pain, or to insert more if many of them had died. Maggots were left in the wound until it looked healthy and X-ray examination showed the bone to be healed. The disadvantages of this treatment were the expense incurred and the pain produced. The advantages were rapid debridement of necrotic material, discovery of hidden sequestra and pockets of pus, stimulation of granulations, and continuous treatment. The period of stay in hospital was shortened. There were 31 lesions in 29 cases; 26 of these were closed, one still required treatment; 2 involved a subsequent amputation and 2 were not traced.

Uleron.—A. Mitchell found that sera and blood transfusions are of very little value in the treatment of the more severe types, and advocated the employment of uleron in acute septic osteomyelitis. From the liability to recurrence he recommended complete subperiosteal resection in suitable cases. After a search for a specific agent likely to influence the staphylococcal septicaemia, he found that in a series of 5 cases uleron was extremely successful in tablet form ($7\frac{1}{2}$ grains). To young children one tablet every 4 hours can be given, and has been administered for several weeks.

Key, J. A. (1938) *J Amer med Ass*, **111**, 2163

Lacy, N. E., and Engel, L. P. (1939) *Arch Otolaryng.*, *Chicago*, **29**, 417.

Maddock, S., and Jensen, D. (1938) *Arch. Surg*, *Chicago*, **37**, 811

Mitchell, A. (1938) *Brit. med J.*, **2**, 1200.

Multiple Myeloma

R. L. Holman recorded fatal anuria and uraemia in a coloured woman, aged 43, with multiple myeloma (plasma-cell type). During life the diagnosis lay between lymphoblastoma of unknown site, Hodgkin's disease of unknown site, and multiple myeloma; radiologically there was a lesion in the spinal column, but the urine did not contain Bence Jones' protein. After a scanty excretion of urine for 12 days complete anuria came on and lasted for 8 days. The necropsy showed that the anuria was due to blocking of the renal tubules by protein casts. The glomeruli were normal, and perhaps the urine excreted into the glomeruli began to precipitate the protein casts when the re-absorption of water in the tubules took place. No reference to the occurrence of anuria in multiple myeloma could be found by the author.

Holman, R. L. (1939) *Arch. Path.*, *Chicago*, **27**, 748.

BRAIN ABSCESS

See also Vol II, p. 597.

Aetiology

Sequel to Tonsillitis

A case of brain abscess following tonsillitis is reported by I. S. Witchell. This condition is comparatively rare, only 9 instances of it having appeared in the liter-

ature since 1921. The patient, who was in hospital, exhibited the usual symptoms of tonsillitis. Fifteen days after the onset of sore throat a swelling behind the left tonsil was incised and pus obtained. A continued sense of fullness over the left sternocleidomastoid muscle led to cervical exploration and the insertion of a drain into the wound. Blood cultures were persistently negative. Temperatures ranged between 104 and 105° F. and a diagnosis of meningitis was made. The patient died 36 days after commencement of the illness. At necropsy, an abscess 3 cm. in diameter and 1 cm. deep was found, immediately over the pituitary.

Witchell, I. S. (1939) *Arch. Otolaryng*, Chicago, **29**, 835.

Treatment

Sulphanilamide

P. C. Bucy reported the successful treatment by sulphanilamide of a case of streptococcal cerebellar abscess in which the surface of the cerebellum was contaminated with infected pus, which escaped from the needle when the abscess was being drained. In the ordinary course of events meningitis would have developed. It was advocated that in future cerebral abscess should be treated by trephining over the abscess, aspiration of pus, and commencing the administration of sulphanilamide. If this suffices, nothing further should be done, if not the abscess should be opened, evacuated, and drained as usual.

Bucy, P. C. (1938) *J. Amer. med. Ass.*, **111**, 1639.

BRAIN: REGIONAL DIAGNOSIS

See also Vol. II, p. 609, and p. 94 of this volume

Lesions of Frontal Lobe

In the monkeys *Macacus mulatta* and *Cercoebus torquatus* a lesion was produced by M. A. Kennard in the grey matter of the frontal cortex. The conclusions drawn from these investigations were as follows. Failure to respond to visual stimuli following lesions of the frontal lobe appears after ablation of area 8, but not of other regions of the frontal cortex. After unilateral ablation of area 8, objects in the contralateral visual field are ignored, and the resultant 'visual' defect in the contralateral homonymous field cannot be differentiated from a true hemianopia except that it is transient. Hand performance contralateral to a lesion of area 8 is also changed. The hand is used less, and effective purposeful movements are not well carried out. The failure to respond to objects seen and objects touched is of the same order. The apparent lack of recognition of objects is due to disturbance of the more complex integrative processes of the frontal lobe, which can account for the alterations in behaviour of these animals.

Kennard, M. A. (1939) *Arch. Neurol. Psychiat.*, Chicago, **41**, 1153.

Lesions of Cerebellum

Arm-Swinging

R. Wartenberg has drawn attention to the relation between unilateral decrease or cessation of arm-swinging in walking and the presence of cerebellar disease. This point was emphasized in the case of a girl of 12 years, who complained of headache and vomiting and showed certain signs diagnostic of cerebellar tumour, including complete loss of pendular movement of the right arm. The diagnosis was confirmed at operation, and a fibrosarcoma was removed from the middle of the right cerebellar hemisphere. Following recovery the arm movement became normal. Some 4 years later the patient came for examination, complaining of dizziness and double vision, and the loss of movement in the arm was again noted. A month later a diagnosis of cyst or recurrence of tumour was made, and confirmed at operation. One branch of the tumour, which was the size of a hen's egg, extended deeply and projected into the fourth ventricle. Special attention given to this sign has aided diagnosis in difficult cases. It was found in one case diagnosed as a tumour on the lower surface of the right cerebellar hemisphere, and which responded to iodine and X-ray treatment. With subsidence of the tumour, the right arm became almost normal. The sign was also present in cases of injury chiefly affecting one side of the

posterior fossa. The particular interest of this involvement of the arm lay in the fact that, although it is recognized as a sign of pyramidal or extrapyramidal disease, in the case quoted it was found in a strictly unilateral injury of the cerebellum.

Wartenberg, R. (1939) *J. Amer. med. Ass.*, **112**, 1454.

Lesions of Temporo-Parietal Region

L. Benedek and L. v. Angyal report the case of a man of 18 who suffered a serious injury in his right temporo-parietal region. Radiological examination showed a fracture in the skull running from the parietal bone down to the occipital bone on the left side, and another on the right side running from the temporal bone into the base of the skull. Extensive fracture was seen in the left temporal bone around the pars acusticus internus. For some time the patient was mentally disturbed. The clinical signs were as follows: (i) spasm of the eyes to the left; (ii) amaurosis in the right eye, hemianopia in the left eye to the right side; function was abolished in the right cochlear nerve and diminished in the left; the right vestibular nerve was excitable, the left not excitable; (iii) disturbance of water-metabolism, sexual desire, and secondary sexual signs; increase of body-weight (from 72.2 kg to 76.2 kg.), slightly increased quantity of sweat; (iv) alteration of character, fits provoked by emotion, (v) thalamus-syndrome: superficial and deep anaesthesia, hemiataxia; hyperpathia for cold; fingers of the right hand in the position characteristic of lesions of the optic thalamus, flexion in the proximal and distal joints, and extension in the middle joint, mild affection of the pyramidal tracts. By assuming that the thalamo-geniculate artery was damaged in addition to the injury in the bones of the skull, all the signs observed in this case may be explained in the following way: (i) Spasm of the eyes to the left resulted from a lesion producing irritation in the posterior visual centre of the temporo-occipital region. (ii) Amaurosis in the right eye and hemianopia in the left eye resulted from a haematoma producing complete destruction of the left optic tract and partial destruction of the right one. Disturbance in the function of the 8th nerve was a direct result of the multiple fractures in the bones. (iii) Endocrine disturbance was a result of lesions in the hypothalamus and hypophysis. (iv) The alteration in character observed in this case probably resulted from an injury to those parts of the brain which are damaged in young persons suffering from epidemic encephalitis when they are affected by alteration of character. (v) Disturbance of sensation, the so-called optic thalamus hand, and the pyramidal signs probably resulted from haemorrhage from the thalamo-geniculate artery.

Benedek, L., and Angyal, L. v. (1939) *Dtsch. Z. Nervenheilk.*, **148**, 196.

Sensory Cortex

Vibratory sensibility.—The question is discussed by H. W. Newman *et al.* as to whether vibratory sense is an entity in itself. The central representation must be localized in the sensory cortex. Its pathway traverses the thalamus, and probably the homolateral posterior columns. The authors used for measurement of the vibratory stimulus an electromagnetic vibrator. They examined the type and location of the end organs involved in the vibratory sense. They concluded that the sensation of vibration may proceed from stimulation of receptors in the skin and in the deeper structures. It is probable that the receptors in the skin are the same as those concerned with the sensation of touch, while those in the deeper tissues are closely related to, if not identical with, the receptors mediating the sense of passive movement.

Newman, H. W., Doupe, J., and Witkna, R. W. (1939) *Brain*, **62**, 31.

Determination of Areas of Hyperpathia

In a paper on localization of intracranial lesions and the determination of areas of hyperpathia (pain lasting longer than the contact of the irritant and tending to spread into adjacent parts), F. H. Lewy described a simple diagnostic method which had been employed in 100 cases, 79 of cerebral tumour, 6 of cerebral abscess, and in a few other conditions, such as subdural haematoma, arachnoiditis, and meningeal scars. The position of these hyperpathic areas could be used for the localization of the lesion. Except in the lower occipital lesions the pain appeared to be referred to the skin over the distribution of the trigeminal nerve. Lesions of the temporal lobe produced hyperpathia behind the ear, in the frontal lobe in the supra-orbital region,

and parietally if in the parietal lobe. Though localization by this method was only approximate in some cases, it was accurate in cerebellar and sphenoidal ridge tumours and especially valuable in the differentiation of supra- and infra-tentorial tumours. Six illustrative cases were quoted and Lewy laid stress on the importance of regarding the sign as a useful supplement to, not a substitute for, the ordinary clinical methods of intracranial localization.

Lewy, F. H. (1939) *Ann. Surg.*, **109**, 28.

BRAIN TUMOUR

See also Vol. II, p. 619, and p. 94 of this volume.

Meningioma

Meningiomas account for 12 to 20 per cent of intracranial new growths. G. Horrax reviewed the symptoms and diagnosis in 60 cases, 46 of which occurred in women and most of which affected the anterior part of the brain. He divided them into 8 main types. (i) Tumours over the cerebral convexities with their dural attachment often at or near the sagittal sinus. Many of these cause local or generalized convulsions, and they can often be seen in X-rays of the skull or after ventriculography. Their typical appearance is of a circular area of thickened bone projecting inward. (ii) Suprasellar meningiomas which press on the optic chiasma and produce the pressure changes typical of enlargement of the pituitary body (iii) Meningiomas arising from the olfactory groove which cause anosmia, optic atrophy on the side of the tumour, papilloedema on the other side, and mental changes. (iv) Orbito-temporal tumours easily diagnosed by the unilateral exophthalmos which they produce and the enormous thickening of the orbital bones on that side. (v) Meningiomas straddling the sagittal sinus, and spreading laterally over both cerebral hemispheres. These tumours produce signs of cortical compression leading eventually to spasticity and paralysis of the limbs (vi) Meningiomas growing from the falx which spread laterally and largely subcortically; this type may be bilateral, and is very vascular and difficult to remove. (vii) Multiple meningiomas. (viii) Meningiomas in unusual places such as the pineal body and the posterior fossa. The surgical treatment of the tumours in this series had an operative mortality of 12.6 per cent.

Horrax, G. (1939) *Arch. Neurol. Psychiat., Chicago*, **41**, 140.

Diffuse Glioblastosis

Diffuse glioblastosis has to be separated from diffuse sclerosis as well as from glioma. R. Kautsky found that the form and structure in the affected parts of the brain were only slightly changed, as demonstrated by microscopical examination. Most of the glial tissue was affected in a certain region of brain, but the functional nervous tissue was preserved in high degree. Only secondary degeneration was observed in the medullary sheath as well as destruction of axis cylinders and ganglion cells. Diffuse glioblastosis is a special form of neoplasm of glial tissue; its characteristic sign is primary diffuse growth, nervous tissue remaining unaffected. Clinical diagnosis of diffuse glioblastosis is extremely difficult. In contrast to disseminated sclerosis, the signs may be explained by affection of one single focus; in contrast to a tumour, however, the signs produced by affection of any focus remain incomplete so that one or the other sign expected from the affection of any one focus may be absent.

Kautsky, R. (1939) *Dtsch. Z. Nervenheilk.*, **148**, 143.

Tumours of Thalamus

The result of clinical and anatomical examination in 6 cases of tumour affecting the thalamus (5 gliomas and one sarcoma) was reported by G. E. Smyth and K. Stern. Thalamic gliomas in a strict sense form a well-defined group. Histologically they appear to take origin from the subependymal glial layer, and hence they are primarily related to the medial areas of the thalamus, to the caudate nucleus, roof of the mid-brain, and to the walls of the lateral ventricles. They invade the brain in a lateral direction, and have little or no tendency to invade the tuber cinereum. Clinically they are characterized by the early onset of mental deterioration and early

conjugate ocular palsies. Objective sensory disturbances are absent or appear late. In the early stage of their development the presence of dementia and iridoplegia may readily suggest general paralysis. In 2 cases in which the thalamus was invaded by tumour from its lateral and ventrolateral aspect, gross sensory disturbances developed early. The differing symptomatology of these 2 groups may be explained by the site and mode of extension of the tumours; in growths invading the thalamus from the ventro-lateral aspect the secondary sensory neuron and its termination are destroyed first; in intrinsic thalamic gliomas, which expand from the medial nuclei laterally, the ventro-lateral areas of the thalamus are invaded late and incompletely.

Smyth, G. E., and Stern, K. (1938) *Bram*, **61**, 339.

Tumours of Third Ventricle

T. M. Nielsen and R. B. Rancy describe the case of a man aged 44, a mathematical and mechanical genius, in whom a change of personality arose, characterized by amnesia, somnolence, and outbursts of anger. Except for slightly increased deep reflexes, no physical abnormal sign was observed in the beginning of the illness. Later on pyramidal reflexes were definitely exaggerated and the basal metabolic rate was lowered. Ventriculography 3 years after the first signs had appeared showed a tumour in the third ventricle as well as dilatation of all the ventricles. The tumour was removed by operation but the patient died 8 hours after the operation. The illness of another patient also started by mental signs. The patient, a man of 30, became confused and disorientated. He lost his memory, pupils were fixed to light; gait was spastic, speech slow, and ataxy was observed. The cerebrospinal fluid was normal, but the pressure was raised. Fully developed choked discs, symmetry of deep reflexes and dorsal plantar reflex on both sides, combined with the characteristic mental signs made the diagnosis of a tumour in the third ventricle probable. Ventriculography showed such a tumour. Death occurred from broncho-pneumonia 12 days after removal of the tumour. The characteristic mental signs observed in a tumour in the third ventricle may perhaps result from pressure on the optic thalamus preventing normal function of the frontal lobes.

Nielsen, T. M., and Rancy, R. B. (1939) *Bull. Los Angeles Neurol. Soc.*, **4**, 1.

Tumours of Fourth Ventricle

Early diagnosis of tumours of the fourth ventricle is difficult because they produce symptoms of increased intracranial pressure but no typical syndrome. In a series of 82 cases W. McK. Craig and J. W. Kernohan found 31 medulloblastomas, 21 ependymomas, 4 oligodendrogliomas, 2 gliomas of the granular layer of the cerebellum, 1 epidermoid cyst, 3 haemangio-endotheliomas, 19 astrocytomas, and 1 papilloma of the choroid plexus. Headache was an initial symptom in 79 of the 82 cases, frontal in 34, occipital in 39. In 67 cases vomiting was an initial symptom, in 19 of these it was projectile. In 64 cases, an early ataxy was present. Among visual difficulties, 31 complained of visual impairment and 55 of diplopia; a choked disc was found in 74 and nystagmus in 61. The correct operative procedure in this condition is a suboccipital craniotomy. The posterior horn of the lateral ventricle is aspirated before opening the dura. After the tumour has been removed, air can be injected into the posterior horn of the lateral ventricle, when it bubbles through into the fourth ventricle, it demonstrates that the aqueduct of Sylvius is patent. Post-operative irradiation is especially important in the case of medulloblastomas and its application to the entire cerebrospinal axis in these cases is sometimes advised, with high voltage roentgen therapy and the administration of a maximal dose to each portal. A series of cerebellar medulloblastomas had an average post-operative life of only 17.3 months. The use of frozen sections and staining with polychrome methylene blue aids speedy differential diagnosis of the tumours at the operating table.

Craig, W. McK., and Kernohan, J. W. (1938) *J. Amer. med. Ass.*, **111**, 2370.

Tumour of Corpus Callosum

J. A. Barré *et al.* report the case of a man of 38 years who suffered from mental disturbance for one year, losing interest in his family and in his work. On examina-

tion, apart from the mental signs, imbalance and fine tremor in hands and face were observed. Examination of the cerebrospinal fluid showed a pressure of 41 cm., albumin 0.50, cells 0.4, and negative Wassermann reaction. Ventriculography disclosed enlargement of the left anterior ventricle. At necropsy a large tumour was found in the corpus callosum, only the most posterior part of which was not destroyed. The psychical signs observed in this case were of special interest, namely impossibility of concentration, increased threshold for sensory impression, and imperviousness to stimuli. In a case of pure frontal tumour these signs are not so well marked, so that they assist in the differential diagnosis between lesions in these 2 sites. The signs of imbalance were different from those in a case of vestibular dysfunction and disappeared for a short time when the patient was asked to walk forward. It was difficult to explain the absence of apraxia. Perhaps the fact that the most posterior part of the corpus callosum was spared was of importance. But it may be that damage to the parietal lobe is of greater importance in the production of apraxia. Tremor in hands and face has also been observed in other cases of tumour in the corpus callosum, and is an important sign.

Barré, J. A., Kabaker, Pernot, and Ledaux (1939) *Rev. neurol.*, **71**, 389.

Tumours of Cerebrum

Cause of Misleading Symptoms

One hundred cases of tumour in the cerebrum were examined by E. Pichler. Symptoms resulting from damage to the brain stem and cranial nerves were observed in 35 cases. Removal of the brain stem over the middle line causing tearing of the pituitary-diencephalon system was supposed to be the cause of symptoms in one case of diabetes mellitus, as well as in one case of diabetes insipidus, and in one case characterized by mental signs. Vegetative disturbance may result from a damaged mesencephalic centre as well as from 'ependymitis blastomatosa'. Homolateral hemiplegia was observed in 5 cases of tumour of the cerebrum. It was produced by impaction of the contra-lateral ventral portion of the crus cerebri, by the tentorium cerebelli, and by marked shifting of the mesencephalon. The corpora quadrigemina were damaged in one case by pressure in the mesencephalon. The mesencephalon, however, was more often affected by projection of the tumour itself or direct pressure produced by cerebellar tumour. A lesion in an optic nerve resulted in one case from a prominent gyrus rectus, and a lesion in the optic tract of another case was produced by a prominent uncus. Paralysis of the sixth nerve was often observed as a distant sign in a case of tumour of the cerebrum, extracerebral lesion of the third nerve was not observed. Argyll Robertson's phenomenon was observed in 8 cases, 4 times combined with anisocoria. Horner's syndrome was observed 3 times. Homolateral trigeminal neuralgia was observed in 3 cases of tumour in the temporal lobe; in one case the trigeminal nerve was affected on both sides. The corneal reflex was disturbed in 8 cases, either on the contralateral side only or more markedly than on the homolateral side. Diminished corneal reflex on the side of the tumour was observed in one case. Pontine symptoms were observed twice in tumour of the cerebrum resulting from pressure in a diagonal direction.

Pichler, E. (1938) *Arch. Psychiat. Nervenkr.*, **110**, 75.

Metastatic Brain Tumours

Metastatic tumours occur in the brain more frequently than was supposed until a few years ago. Epitheliomas from primaries in lungs and mammary glands have been described. R. S. Romay observed most frequently metastasis from the lungs and adrenal glands. All these tumours produce one single or multiple metastases, either in the meninges or in the white or grey matter in the brain. Neoplasms in the apex of the lungs were usually spread by the lymphatics. Epithelioma in the adrenal gland has a definite tendency to metastasize in the cerebellum. A metastatic tumour presents no characteristic symptom of its own, as maintained by some authors. Hypertension and papilloedema, as with a primary tumour, are usually the first signs. Primary tumours often produced no symptom before metastasis occurred. A metastatic tumour infiltrates nervous tissue and destroys it completely.

Romay, R. S. (1939) *Arch. argent. Neurol.*, **20**, 89.

Prognosis

Personality Changes after Operation

G. Rylander examined 32 patients after partial excision of the frontal lobes performed for a tumour or an abscess. The author concludes that mental changes occur after excision of parts of the frontal lobes. Generally the change was not of such a degree as to destroy the subject's ability to lead a normal social existence, but it may be serious to persons doing intellectual work. Consequently the mental sequelae, however important they may appear to the psychiatrist, do not represent any contra-indication to the partial excision of the frontal lobes in urgent cases, in which they are far outweighed by the advantages of the operation.

Rylander, G. (1939) *Acta psychiat., Kbh.*, **20**, 327.

Diagnosis

Ventriculography

Ventriculography with injection of air into the ventricles does not give sufficient information, as the ventricles do not become completely filled in every case, and the lateral and posterior borders of the third ventricle do not become clearly visible. By injecting lipiodol into the ventricles their exact form can be observed. Cases of arachnoiditis, tumours of the cerebral hemispheres, suprasellar meningiomas, pituitary tumours, brain stem and cerebellar tumours, and tumours in the ponto-cerebellar region and fourth ventricle were examined by this method by Y. Piette.

Piette, Y. (1939) *Zbl. Neurochirurgie*, **4**, 15.

Differential Diagnosis

From General Paralysis or Tabes Dorsalis

T. Ruesch states that a brain tumour may sometimes be mistaken for general paralysis or tabes dorsalis as the physical and psychical signs may sometimes be identical. Optic atrophy without papilloedema observed in a case of tumour of the pituitary body or at the base of the frontal lobe may erroneously be diagnosed as a sign of tabes dorsalis in the first place, if the visual fields are not diminished. As a result of retrobulbar neuritis pupil reactions may be slow, suggesting the Argyll Robertson phenomenon. Increased cerebral pressure may cause diminution of reflexes as in the first stage of tabes dorsalis. Psychical signs in a case of brain tumour may be similar to those observed in a case of general paralysis. Examination of the cerebrospinal fluid is valuable in the differential diagnosis, as the Wassermann reaction is positive in a case of luetic affection and the number of cells is increased, whereas in a case of brain tumour the number of cells usually is normal or only slightly increased, but the protein usually is raised. X-ray examination of the skull and ventriculography may be helpful for the diagnosis of a condition producing diminution in the space in the skull.

Ruesch, T. (1939) *Schweiz. Arch. Neurol. Psychiat.*, **43**, 149.

Treatment

Bladder Mucosa

P. Bezza described 3 cases of gaps in the cranial vault following cerebral operations, in which the gaps were filled with bladder mucosa. The results obtained were excellent; in about 90 days there was a complete new formation of bone, demonstrable radiographically. The author reviewed the literature on this subject, stating that many authors have discovered the osteogenic powers of the bladder wall, especially when the mucosa was turned outside, and he recommended its use in filling bony gaps wherever they arise.

Bezza, P. (1939) *Arch. ital. Chir.*, **55**, 405.

BREAST DISEASES

See also Vol. II, p. 657, and pp. 35 and 109 of this volume.

Congenital Lesions

Treatment

Surgical.—According to H. Neuffer the main difficulty in plastic operations performed on the breast for hyperplasia and ptosis is the prevention of necrosis of

the nipples. His method, which was successful in 40 cases, preserves normal sensation and erectibility of the nipples. A superficial incision was made round the areola in the desired position and a second parallel incision was made about 3 cm. distant. From this band the epidermis and upper corium only were separated. The outer incision was then deepened to the subcutis, where the plastic operation was performed. The areola of the nipple was now surrounded by a 'perimamillar cutis ring' from which only the epidermis and upper layer of the corium are absent. The areola of the nipple maintains its new site without any further fixation. The fine blood vessels, lymphatics, nervous fibres, and the muscles of the cutis are preserved. Histological examination showed that nerves, muscles, and blood vessels of the subcutis had not been touched.

Neuffer, H. (1938) *Wien. klin. Wschr.*, **51**, 1312.

Hypertrophy of Male Breast

Treatment

Testosterone.—W. J. Hoffman treated 28 male patients, between the ages of 11 and 73 years, with unilateral or bilateral enlarged mammary glands with testosterone acetate or propionate injections, the first 6 patients being given 5 mg. twice a week; in subsequent cases, after 6 months, the dosage was increased to 25 mg. twice a week. Complete retrogression occurred in 14 cases, and in 9 retrogression followed to an extent of more than 75 per cent. The enlarged mammary glands reach a maximum size at puberty, and may be associated with malignant disease, atrophy of the testis, or castration, and may occur in old age when sexual activity is declining. The possibility that the mammary hypertrophy might be due to lack of the male hormone led to the trial of hormonal treatment. It was pointed out that most of the cases in adolescents underwent spontaneous retrogression.

Hoffman, W. J. (1939) *Amer. J. Cancer*, **36**, 247.

Inflammations

Plasma-Cell Mastitis

J. K. Miller reviewed plasma-cell mastitis which is a subacute or chronic inflammation of the breast characterized by a rich plasma-cell exudate. Actiologically it is confined to multiparous women, the average time elapsing since the last lactation being 4 years. It may be associated with defective breast drainage. Symptomatically it may be difficult to distinguish from carcinoma, the mass being either very firm or hard on section; the ducts are dilated and tortuous with cysts containing greyish creamy matter. The histological picture is characterized by inflammatory granulation tissue which presents a preponderance, and frequently almost a pure culture of plasma cells. There may be an accompanying polymorphonuclear infiltration. Differentiation must also be made from traumatic fat necrosis, from syphilis, from the simple forms of subacute and chronic mastitis, and from tuberculosis, which it may suggest by its fibroblastic and giant-cell formation. The condition should be considered pre-cancerous, and treated as such.

Chronic Mastitis

Prognosis.—W. Sampson Handley reported cases of 5 sisters suffering from mastitis or cancer of the breast whose grandmother and mother had both died of cancerous conditions. From the studies of these and other cases he concluded that chronic mastitis was a precancerous condition which is often amenable to X-ray or radium therapy which may therefore be a prophylactic against cancer. After X-ray treatment the patients should be observed at 3 or 6 month intervals as the protection conferred is not permanent and cancer may develop. In the event of cancer developing Handley considered radical amputation with the application of radium to the internal mammary glands and subsequent moderate X-ray therapy to be the treatment of choice. Five radical operations for breast cancer were performed and additionally two mastectomies, the first for early cancer, the second for precancerous mastitis. Two of the sisters died of breast cancer 11 and 9 years after operation; 3 still survive. The clinical signs that cancer is approaching in a breast which is already the seat of chronic mastitis were divided by Handley into 2 groups: signs in the nipple and signs in the breast. Those in the nipple include retraction of one or more duct orifices without retraction of the nipple; serous or blood-stained discharge from the nipple; deviation of the axis of the nipple; elevation, flattening,

or retraction of the nipple; and white or black dots on the nipple from which plugs of degenerated epithelium can sometimes be squeezed. In the breast the signs consist of the mastitis becoming cystic; tortuous cords representing the main ducts near the nipple in the mastitic area; and occasional adhesion of the breast to the skin or pectoral fascia, this being seen only in fully developed carcinoma. The author is not in agreement with the treatment of chronic mastitis by oestrin injections. He has been a consistent supporter for 30 years of breast irradiation in these cases.

H. J. B. Atkins finds that in the mastitis clinic at Guy's Hospital where 170 cases of mastitis, many of long duration, have been investigated none has developed carcinoma within the two and a half years' life of the clinic. It is certain in his opinion that carcinoma follows mastitis in a strikingly small proportion of cases, in spite of the nature of the accompanying epithelial changes, which histologically are precancerous in type. The fibrosis which is part of the disease may have a protective function against neoplastic disease.

Atkins, H. J. B. (1939) *Brit. med. J.*, **1**, 866.

Handley, W. S. (1938) *Brit. med. J.*, **2**, 113.

Miller, J. K. (1939) *Amer. J. Surg.*, **43**, 788.

Fat Necrosis

Differential Diagnosis from Carcinoma

The importance of differentiating fat-necrosis granuloma of the breast from carcinoma is emphasized by S. F. Livingston and M. Lederer. Two case reports are given of fat necrosis. The authors quote the view of Lee and Adair that it occurs in middle-aged and obese women, that the breasts are unusually large; that there is a history of trauma in 70 per cent of cases; that the tumour is painless, usually stony hard, and may be adherent to the skin or deep fascia. Retraction of the nipple occurs in 20 per cent of the cases. The correct diagnosis can frequently be made if the surgeon keeps in mind the gross appearance of the lesion, but, clinically, fat necrosis resembles carcinoma more closely than other benign lesions. According to Keynes 'fat necrosis of the breast is not a lesion of the mammary gland proper, but the fat which overlies or infiltrates the mammary gland in later life'. Treatment consists of local excision of the tumour.

Livingston, S. F., and Lederer, M. (1939) *Surg. Gynec. Obstet.*, **68**, 230.

Malignant Tumours

Carcinoma

Classification.—A plea for a uniform system of clinico-pathological classification of mammary carcinoma, as has been done for cancer of the cervix uteri, with a view to the estimation of prognosis and for the comparison of the various methods of treatment, surgical and radiological, in comparable series of cases, has been made by R. W. Raven. The proposed clinical classification was based upon a correlation of the interrelated and pathological aspects of mammary cancer. A satisfactory classification must be based on the following clinico-pathological findings: (i) The local condition; involvement or not of the skin, of the pectoral fascia, the pectoral muscle, and the ribs. (ii) Of the regional lymph nodes; the axillary, supraclavicular, mediastinal. (iii) Of distant structures; the visceral and bony metastases. The stage of the disease in the breast was indicated by a number (for example I) and the stage of the disease in the regional lymph nodes indicated by a letter (for example, a); if the disease had spread to the perinodal connective tissues a dash (') was placed after the letter (for example a'); if the disease had spread to other organs of the body, then the first 2 letters of the organ or organs involved were added (for example, lu-lung, li-liver). The author defines the stages as follows. Stage I. Carcinoma strictly confined to the breast. Stage II. Carcinoma infiltrating the pectoralis fascia (stage II fascia). Stage III. Carcinoma infiltrating the pectoralis muscle (stage III muscle). Carcinoma ulcerating through the skin (stage III ulcer). Stage IV. Carcinoma infiltrating the ribs or costal cartilage or sternum (stage IV bone). Carcinoma infiltrating the whole breast with *peau d'orange* and/or infiltration of underlying pectoralis fascia and muscle (stage IV whole breast). The assessment of the stage of disease in the regional lymph nodes and perinodal connective tissues was arranged in 5 stages. Stage a: Involvement of the lymph nodes under the lower border of the pectoralis major muscle. Stage b: Involvement of lymph nodes under

the tendon of insertion of the pectoralis major. Stage c: Involvement of the lymph nodes under the tendon of the pectoralis minor muscle. Stage d: Involvement of the supraclavicular lymph nodes involved. Stage e: Involvement of the mediastinal lymph nodes.

Diffuse metastases in skeleton.—J. F. P. Lamarque discussed diffuse metastasis in the skeleton of mammary carcinoma, by which must be understood wide-spread metastasis in the skull, spine, ribs, pelvis, and the proximal extremities of the limbs; it was not the same as multiple metastases. As thus defined the number of cases was considerably reduced, among about 1,000 patients treated since 1923 in the anti-cancer centre of Montpellier, Lamarque had seen 3 cases only. As more cases had been discovered recently by radiological diagnosis, it had been suggested that X-ray treatment might be responsible; but this seemed improbable, because generalization occurred in patients who had never been X-rayed or operated upon, and in those who had been operated upon but not X-rayed, as in Lamarque's 3 cases. If more cases were seen now, it might well be that more patients, though not cured, survived longer, and detection of bony lesions was more efficient. Clinically, the pain varied in intensity, but might be intolerable, fractures were frequent, but united well; bony deformities were common. The course of the disease was not steadily progressive, exacerbations of local pain and swelling with a raised temperature might be followed by a calm period of well-being. In contrast to the diffuse osteoplastic metastases of primary prostatic carcinoma, the generalization of mammary carcinoma was osteolytic, and radiologically might show regularly oval areas, resembling those in generalized osteitis fibrosa cystica, or diffuse alterations of structure giving a cottony speckled appearance, simulating multiple myeloma. The blood picture might be normal, or present several forms of anaemia. The calcium metabolism might also vary: the calcium content of the blood might be increased, and the parathyroids, though not altered to the naked eye, might show hyperplasia as evidence of over-activity. Even if some cases of the skeletal carcinomatosis were radio-resistant, the immediate results of radium treatment were good.

Metastatic calcification.—J. W. Egovalle reported a case of metastatic calcification in mammary carcinoma involving the skeleton. This condition was described in 1855 by R. Virchow as super-saturation of the blood with calcium and deposits of calcium in parts of the body otherwise normal. The patient, aged 30, a multipara, was admitted to hospital with a history of increasing weakness and attacks of severe shooting pains in the shoulders, back, and lumbar region, markedly aggravated by muscular exertion. A diagnosis of multiple myeloma was made from the radiographic appearances, until a biopsy from a lesion in a rib showed that it was an adenocarcinoma, probably secondary to a tumour of the breast. The blood and urine did not contain Bence Jones' protein. The patient died 3 months after the onset of symptoms. Necropsy, performed one hour after death, showed a primary carcinoma of the right mamma and metastases in the spine and ribs. The heart weighed 350 g. and the endocardium of the dilated left auricle was covered with a brittle fragmented material like egg-shell. Along the attachment of the aortic cusps and scattered along the intima of the aorta were a few small calcified plaques. Sections of lung showed fibrosed and thickened alveolar septa containing calcium granules. There was metastatic calcification in the media of the pulmonary artery, in the bronchiolar submucosa, and in the glomeruli, and calcium casts within dilated convoluted tubules of the kidney, the lining epithelium being swollen, granular, and often detached. Examination of the parathyroids justified the opinion that the hypercalcaemia was not due to over-activity of the parathyroids.

X-ray therapy.—L. G. Allen discussed the problem of radiation therapy in carcinoma of the breast. He accedes to the popular view that a good surgical operation is better than poor radiation therapy but he considers that the reverse also holds good. He concluded that conservative Stage I cases of slowly-growing breast cancer occurring at the age of 40 years are statistically a primarily surgical problem. If the tumour regression does not occur promptly, even after raising the daily radiation intensity from 200 to 400 or 600 *r* measured on the skin by two fields for a minimal total of 3,500 *r* in 10 days, it should be assumed that the tumour is relatively radio-resistant and is of a type which more often metastasizes late and demands surgery as the primary method of treatment. In view of the prevailing beliefs concerning the ovarian influence on the development of cancer of the breast, the author considers that ovarian sterilization, as a pre-operative and post-operative prophylactic measure, is fully justified in order to prevent future pregnancies and particularly

in avoiding the harmful influence of internal ovarian secretion associated with the menstrual function.

Mixed Tumour

G. R. Tudhope gave a full description of a complex mammary tumour, somewhat resembling a malignant embryoma in a woman aged 63. It was a large irregularly outlined growth with 3 lobes, and contained carcinomatous and sarcomatous elements diffusely infiltrating the stroma of an intracanalicular fibro-adenoma from the epithelium of which the carcinoma arose. The tumour also contained cartilage, the nature of which was fully discussed; it was concluded that mucinoid degeneration of the stroma had produced an epithelial pseudo-cartilage, resembling that in mixed parotid tumours, and that in addition true cartilage and osteoid tissue had resulted from metaplasia of the cells of the stroma.

- Allen, L. G. (1939) *Radiology*, **32**, 63.
 Egoilve, J. W. (1938) *Arch. Path.*, **26**, 1047.
 Lamarque, J. F. P. (1939) *Brit. J. Radiol.*, **12**, 321.
 Raven, R. W. (1939) *Brit. med. J.*, **1**, 611.
 Tudhope, G. R. (1939) *J. Path. Bact.*, **48**, 491.
 Virchow, R. (1855) *Virchows Arch.*, **8**, 108

Cysts of the Breast

Under fibrocystic disease of the breast, B. A. Goodman included such terms as chronic cystic mastitis, Schimmelbusch's disease, and mazoplasia, all different names for the same entity. He divided the condition into 3 types, (i) the predominantly cystic, (ii) the predominantly fibrous, and (iii) that in which the cystic and fibrous elements were approximately equal in amount. At first thought to be of nervous origin, it is now considered that it is a clinical state due to some upset of the endocrine functions. More common in non-parous women, it is often accompanied by morbid pelvic conditions, such as ovarian cysts and fibroids. It is doubtful whether fibrocystic disease is precancerous, one observer having found only 1 per cent of cases developing cancer. The best method of diagnosis is careful palpation aided by transillumination which distinguishes the cysts from solid tumours. Radiographic examination is also helpful. Supporting the breast may alleviate the symptoms, and removal of septic foci may improve the condition. Diathermy and short-wave therapy have as yet received little attention. If pelvic disease is present its cure often relieves the mammary condition. Endocrine disorder calls for appropriate endocrine therapy, the injection of gonadotrophic substances being a more sure and successful method than their oral administration. Surgery must be resorted to if other methods fail.

- Goodman, B. A. (1939) *Arch. Surg., Chicago*, **38**, 917.

Hormones in Relation to the Breast

C. H. Birnberg *et al.* discussed the action of oestrone and progesterone upon the breast. Growth of ducts, tubules, and periductal fibrous tissue is stimulated by oestrone, the hormone of the ovarian follicle, and a similar effect is exercised by progesterone upon the secretory glands at the ends of the tubules, with a resulting production of secretion (not milk). Should the balance between these 2 hormones become disturbed, as happens at the menopause, pain, accompanied in some cases by nodular masses, occurs in the breast. Simultaneous injections of oestrone and progesterone result in marked development of duct and acinar systems. Milk secretion, however, depends on the influence of the pituitary, after the breast has been sufficiently prepared and stimulated by the ovarian follicular and corpus luteum hormones. Similarity of response is shown by the breast and the uterus during the menstrual cycle. In 14 cases of breast dyscrasias the authors determined by serial prolactin and oestrone determinations and endometrial biopsies which hormone was lacking and administered it to the patient with good results.

- Birnberg, C. H., Kurzrok, L., and Livingston, S. (1938) *Amer. J. Surg.*, **41**, 39.

BRONCHIECTASIS, BRONCHIOLECTASIS AND BRONCHIAL SPIROCHAETOSIS

See also Vol. II, p. 682; Cumulative Supplement, Key Nos. 199-201; and p. 114 of this volume.

Bronchiectasis

Aetiology

S. H. Watson and C. S. Kibler (1938) observed that many of their patients with bronchiectasis had some allergic manifestation such as hay fever or eczema. The fundamental basis for chronic sinusitis is an allergic rhinitis, and bronchiectasis is often an associated condition. They investigated the bronchial secretions of all patients with bronchiectasis and found that the majority of them contained an excess of eosinophils—10 per cent or more. They found from skin and other tests that a diagnosis of allergy could be made in 90 per cent of their bronchiectatic patients. The authors divided their cases into 4 types, and reported a case of each type. The first, although diagnosed as bronchiectasis elsewhere, was shown on X-ray examination to be a basal allergic bronchitis, the skiagram showing no bronchial dilatation. The second type consisted of slight bronchiectasis, the third of moderate, and the fourth of advanced bronchiectasis. In all 4 types strong evidence of allergy was found, and it was considered that each was a forerunner of the other, and, if basal allergic bronchitis was recognized and treated early, bronchiectasis of the allergic kind would not occur. The patients were treated by means of desensitization and elimination diet, the best results being obtained in the early stages.

Further observations of Watson and Kibler (1939) confirmed their previous assumption that bronchiectasis has an aetiological background of allergy, and it is considered that the relation of bronchiectasis with sinusitis is explained by this fact. In a series of 46 cases studied, 31 had an associated sinusitis. Hay fever, polyps, or nasal allergy was present in 27 and some history of asthma in 15. A radiological examination of several cases which presented all the symptoms of bronchiectasis failed to show bronchial dilatation with lipiodol injections, and these were diagnosed as basal allergic bronchitis. Skin tests by the scratch method were performed, and, if these failed to produce a reaction, the intracutaneous method was used. A positive reaction was obtained in 38 of the cases under review. High eosinophil counts were present in the nasal or bronchial secretions, sometimes even in patients giving negative skin tests.

Prognosis

After surgical treatment.—J. V. Bohrer and C. W. Lester described the results of 10 cases of bronchiectasis in children which were dealt with surgically. Three were treated by pneumonectomy and the rest by lobectomy. Postural deformities did not occur, and neither phrenic resection nor thoracoplasty was necessary. No cardiac respiratory disturbance was noted in any of these cases. The diaphragm was elevated and the mediastinum shifted, but without functional upset. Physical development after operation was normal if all diseased areas were eradicated. Surgery gave better results in children than in adults. The mortality with conscientious medical treatment in children up to the age of 20 is very small. Therefore the main reasons for operation are to prevent adult bronchiectasis and to avoid social ostracism.

Treatment

Lobectomy.—D. E. Ross quoted Archibald's classification of bronchiectasis into 3 stages: the first is a bronchitis, with no bronchographic changes; the second shows cylindrical and saccular dilatation, and is characterized clinically by cough and sputum which fails to yield anaerobic organisms; and the third, or foetid, stage is marked by quantities of foul-smelling sputum containing anaerobes, and by the presence of bronchiectatic cavities. If bilateral lobectomy is performed before the third stage is reached, the chances of a fatal empyema are considerably lessened. As the production of adhesions which exposes a smaller area of pleura to infection is considered useful, a two-stage operation is advised. Spinal anaesthesia, in conjunction with the customary pre-operative dose of scopolamine and morphine, is suitable. Two successful supporting cases are described.

X-irradiation.—Treatment of bronchiectasis with X-rays was performed with

considerable success by M. Berck and W. Harris. The cases selected were graded in 3 groups: non-foul catarrhal bronchiectasis; foul suppurative bronchiectasis secondary to chronic lung abscess which had already been made the subject of operation; and foul suppurative bronchiectasis. The patients in the first group showed an aggravated form of chronic bronchitis, with additional catarrhal infection. The second group is self-explanatory. In the third were placed those patients who were seriously ill with distressing cough and foul sputum which was less profuse than in the second group, and who revealed less marked parenchymal involvement. The mortality rate from operative procedures in the last 2 groups is high. The X-ray therapy was given over a period of approximately 3 months. All the diseased areas were cross-fired and the total dosage given was approximately 1,500 *r* through each portal of entry. The technique adopted was 180 to 200 kv. with a focal skin distance of 50 cm., filtered through 0.5 mm. copper and 1.0 mm. aluminium. The average size of the field treated was 10 × 15 cm. and 75 *r* were given at each treatment to 2 or 3 fields.

In the first group, 3 out of 5 patients were greatly improved; in the second 10 out of 20, and in the third, 18 out of 40 showed equivalent improvement. The criterion of success was decreased expectoration, and those who responded to treatment showed reductions in sputum from 20 fluid ounces to even as little as one fluid ounce. A follow-up of these cases for periods of from one to 6 years showed arrest of the symptoms of chronic toxicity, foul expectoration, and cough in a large percentage of cases.

Combined method.—J. J. Singer, after emphasizing the value of rest and postural drainage in cases of bronchiectasis and the curative results obtained with a lobectomy, suggests 3 measures which occasionally show successes: (i) the intravenous injection of neoarsphenamine in similar doses to those employed in the treatment of syphilis; (ii) bronchial irrigation through a bronchoscope or by a soft rubber Coudé catheter employing a hypertonic saline solution; and (iii) the intrabronchial injection of 10 to 20 c.cm. of lipiodol once a week for 3 or 4 weeks. Care must be taken to avoid any mechanical disturbance and to warm the lipiodol to body heat before its introduction.

Berck, M., and Harris, W. (1939) *J. Radol.*, **32**, 693.

Bohrer, J. V., and Lester, C. W. (1939) *J. thorac. Surg.*, **8**, 412.

Ross, D. E. (1938) *Canad. med. Ass. J.*, **39**, 459.

Singer, J. J. (1939) *Surg. Gynec. Obstet.*, **68**, 327.

Watson, S. H., and Kibler, C. S. (1938) *J. Amer. med. Ass.*, **111**, 394.

— — (1939) *J. Allergy*, **10**, 364.

BRONCHITIS AND BRONCHO-PNEUMONIA

See also Vol. II, p. 696, and Cumulative Supplement, Key Nos. 202-207.

Bronchitis

Treatment

Prontosil soluble inhalations.—H. Franke treated about 100 cases of various types of bronchitis with inhalation of prontosil soluble (10 c.cm. of a 2.5 per cent solution for 15 to 20 minutes). He found no complications or side effects. The substance appears in the urine 10 minutes after inhalation and is nearly completely excreted after 1½ hours. The treatment gives excellent results after 2 to 3 inhalations. The quantity of sputum is reduced. Cough disappears as well as irritating subjective symptoms in the larynx. There is also an increase in the vital capacity of the lungs (about 1,000 c.cm.). Indications for the treatment are acute bronchitis (cure in 1 to 2 days after inhalation), chronic (muco-purulent) bronchitis, and bronchiectasis.

Franke, H. (1939) *Munch. med. Wschr.*, **86**, 494.

Broncho-Pneumonia

Bacteriology

A new filtrable agent associated with respiratory infections was described by J. Stokes, Jr., A. S. Kenney, and D. R. Shaw. It was isolated from washings of the throat and nose of 2 children, the clinical features of whom were reported else-

where by Reimann. Laboratory experiments suggested that there was a new filtrable agent which caused disease (broncho-pneumonia and cerebral symptoms) in mice, guinea-pigs, and possibly in ferrets, and may have been in part responsible for the disease of the patients. It was not the virus of epidemic influenza, of lymphocytic chorio-meningitis, or of meningo-pneumonitis.

Reimann, H. A. (1938) *J. Amer. med. Ass.*, **111**, 2377.

Stokes, J., Jr., Kenney, A. S., and Shaw, D. R. (1939) *Trans. Coll. Phys. Philad.*, 4th ser. **6**, 329.

BRONZING OF THE SKIN

See also Vol. II, p. 711, and Cumulative Supplement, Key No. 208.

Aetiology

P. Manson-Bahr and O. N. Ransford reported cases of abnormal pigmentation occurring in the tropics due to acquired or inborn errors of metabolism; these included cases of carotinaemia with the characteristic yellow pigmentation, in one case an abnormal, mainly vegetable, diet may have been the source of the carotene; another patient was the subject of diabetes mellitus. Haemochromatosis occurred in 2 patients; the hepatic enlargement was in one due to chronic hepatitis after amoebic dysentery, and in the other to cirrhosis associated with *Schistosoma mansoni* infection. They also recorded the case of a man with alkaptonuria, resident in East Africa for many years, who was known to have had this inborn error of metabolism from boyhood and whose sister was similarly affected; he had had various other diseases including malaria, amoebic dysentery, and syphilis. It was suggested that haemochromatosis and alkaptonuria predispose individuals to tropical diseases and that those with these conditions are unsuitable for residence in the tropics.

Manson-Bahr, P., and Ransford, O. N. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 395.

BURNS AND SCALDS

See also Vol. II, p. 719.

Pathology

T. H. Belt reported 4 cases of death from burns, all of which showed characteristic hepatic changes identical with those of yellow fever, and consisting macroscopically of cloudy swelling and yellow coloration of the parenchyma. Histologically there was wide-spread mid-zonal necrosis, Councilman bodies in the cytoplasm, and intranuclear inclusion bodies. There were also signs of acute toxæmia in other organs, such as the heart, kidneys, and spleen. In all 4 cases the burns were extensive and were treated with tannic acid, the patients dying within 4 days of injury. Necropsy was performed within a few hours of death in every case.

Belt, T. H. (1939) *J. Path. Bact.*, **48**, 493.

Special Types of Burns

Hydrofluoric Acid Burns

A. T. Jones reported 12 cases of hydrofluoric acid burns which were successfully treated. Immediately after burning, the part should be immersed in hot saturated sodium bicarbonate solution, or if more practicable the solution should be applied to it. This is followed by the application of a paste of magnesium oxide and glycerin. Some of the cases in this series received an injection of a 10 per cent sterile solution of calcium gluconate into and under the coagulum formed by the burn. This measure reduced the pain and was followed by twice-daily applications of the magnesium oxide paste for 5 or 6 days. After this, a boric acid ointment can be used and then ichthammol ointment to complete the healing. Burns resulting from hydrofluoric acid are intensely painful, and the pain may be delayed for some hours. A tough eschar forms, and the skin under it continues to be destroyed for some days after the burn, as the action of the acid is progressive. The author also reported 3 cases of conjunctivitis probably due to hydrofluoric acid. These were successfully treated by

frequent irrigation with warm saline followed by the instillation of 5 per cent prontosil soluble ointment.

Cement Burns

J. M. Meherin and T. P. Schomaker treated 60 cement burns in a period of a year and a half. It was noted that pain, usually occurring 2 or 3 days after the burn was contracted, was the symptom which first brought the patient under medical care, and that during the interim the lesion had become analogous to an ulcer and should be treated as such. Infection complicating the burns was frequent, and amounted to 20 per cent of the series. A greyish-brown soft scab was usually present, firmly adherent to the underlying tissues. Necrosis was apparent. Although the classical treatment advised consists of scrubbing with soap and water, this was not considered practicable as it necessitated a general anaesthetic. The forming of an eschar by tannic acid or silver nitrate is not ideal treatment because of infection and the sealing in of the offending chemicals. The application of a soothing ointment proved the most successful measure. After 24 hours the crust was loosened, leaving a ragged ulcer. Following the appearance of clean granulations, an ointment containing cod-liver oil was found to promote healing. Prophylactic treatment of cement burns should include lavage and showers applied to all exposed parts immediately after cessation of work; application of lanolin to the parts most frequently exposed would also be effective but somewhat impracticable. Clean dry boots and gloves, changed at frequent intervals, are helpful.

Jones, A. T. (1939) *J. industr. Hyg.*, **21**, 205.

Meherin, J. M., and Schomaker, T. P. (1939) *J. Amer. med. Ass.*, **112**, 1322.

Treatment

In Children

H. M. Blackfield and L. Goldman described a method of treating burns in children, and claimed this to be the most satisfactory therapy yet evolved. In all cases shock was treated before any local therapy was commenced, and this included a transfusion in all cases of severe burns. Next, the patient was immersed in a tannic acid bath which had been prepared by adding to warm water (90 to 100° F.) enough tannic acid powder to give a muddy appearance. In some cases the water needed to be changed 2 or 3 times before the removal of the debris was completed. All blebs, previous ointments, and pieces of necrotic tissue were removed with sterile scissors, and the surrounding skin was gently washed with green soap and water. The next step, after the patient had been dried with sterile towels, was to apply a 10 per cent solution of silver nitrate on gauze over the burned area. This rapidly formed a satisfactory eschar, an improvement on tannic acid spray therapy, where the formation of an eschar may take from 12 to 72 hours. The authors urge that this time factor in treating burns is all-important if subsequent infection and sepsis are to be avoided. After the application of the silver nitrate the patient was laid on a sterile sheet beneath a cradle and kept warm by radiant heat. A 1 per cent aqueous solution of gentian violet was applied to the entire burned area and edges several times a day at the beginning of treatment. The eschar was found to loosen after 7 to 14 days, and was trimmed away, gentian violet being applied. If a portion of the eschar remained after 3 weeks, it was removed under a light anaesthetic, and, after preliminary preparations which included daily tub baths, saline compresses, and the use of diluted solution of sodium hypochlorite or azochloramid, the injured area was covered with skin grafts. Where possible, grafts of intermediate thickness were employed.

Adrenal Cortical Hormone and Vitamin C

M. Einhauser is of the opinion that 2 processes are of paramount importance in severe burns: (i) the toxic effect of products of protein decomposition; and (ii) the disturbance of the permeability between blood and tissues due to these toxic substances. The permeability of the tissues (which is the same as their 'vitality') is associated with the effect of the adrenal cortical hormone. The symptoms of deprivation of the adrenal glands and of severe burns are, as far as the blood circulation is concerned, the same. There is a steady stream of water into the tissues with a concentration of the blood; the blood volume is reduced and blood pressure falls. Sodium passes from the blood into the tissues and potassium from the tissues into

the blood. In severe burns there is anatomical damage of the adrenal glands as well as of other organs due to the toxic effect of the protein products. The author showed by animal experiments that injections of adrenal hormone or of vitamin C, which has a similar effect, saved 50 per cent of burned animals when 100 per cent of the controls died. In a case of a boy suffering from an electric burn affecting 55 per cent of his body surface, tannic acid treatment was combined with the injection of adrenal hormone and vitamin C. Doses of an extract corresponding to 20 g. of fresh adrenal cortex were injected 5 times daily. In addition 2 injections of ascorbic acid totalling 1,500 mg. were given daily. The patient's condition appeared critical during the second week. The dose was reduced after 2 weeks to 3 injections of adrenal hormone and to 500 mg. of vitamin C. The condition improved, and after 10 months nearly all the burns were healed; the weight and general condition of health were very good.

Tannic Acid and Ferric Chloride

H. Poyner described a modification of the present method of treating industrial burns; this he had employed in 250 cases. To the burned area was first applied a fresh 5 per cent solution of tannic acid which was immediately wiped with a 5 per cent aqueous solution of ferric chloride. A black coagulum was formed which required no dressing and the patient obtained relief from pain. If vesicles appeared they were opened and treated similarly. Subsequent treatment was the same as that employed with tannic acid alone. In view of the considerable loss of blood serum from burns, it was recommended that intravenous infusion should be undertaken immediately, and when the haemoglobin readings rose over 10 per cent within 48 hours transfusion should be performed. When necessary skin grafting was carried out as soon as the crusts peeled off. In regions normally covered by clothing, pinch grafts are recommended, but in facial burns, pedicle, whole thickness, or split grafts are preferable.

Infra-Red Irradiation

J. Gautier published his observations on the infra-red treatment of burns, claiming that this method is superior to all existing forms of treatment, even including tannic acid. The first observations of the author were based on a number of cases published in 1938. The general treatment of burns remains the same, shock is abated, and the patient put to bed. As soon as possible after the injury, the patient is put under an infra-red lamp and in half an hour the pain disappears. The vesicle is punctured and loose epithelium is removed. After one hour's irradiation a heat cradle is substituted to keep the patient warm. No dressing is applied to the burnt parts. Two daily irradiations each lasting about one hour are advocated by the author, and it is contended that, after the second of these, crust-formation begins and exudation stops. Pain is completely abolished and no analgesic need be given. In the author's view, further experiments are necessary to establish definitely the value of this treatment in severe burns.

Skin Grafting

Deep scars from burns produce contractures which may lead to great deformity, especially when the scars lie over joints. Treatment is difficult because the trauma of attempted exercises in physiotherapy leads to ulceration, and complete skin grafts after removal of the scar rarely take. H. Conway devised a method of making a 'relaxation' incision at the point where the scar exerts the greatest force, and in the resulting elliptical space he grafted a piece of whole skin. This was kept completely immobilized after operation. He reported 3 cases of burns of the trunk and thigh which were so treated. They were all successful, giving softer scars and greater freedom of movement.

Blackfield, H. M., and Goldman, L. (1939) *J. Amer. med. Ass.*, **112**, 2235.

Conway, H. (1939) *Ann. Surg.*, **109**, 286.

Einhauser, M. (1939) *Munch. med. Wschr.*, **86**, 441.

Gautier, J. (1939) *Pr. méd.*, **47**, 139.

Poyner, H. (1938) *Amer. J. Surg.*, **42**, 744.

CAISSON DISEASE

See also Vol. II, p. 730.

Treatment

O. D. Yarbrough and A. R. Behnke stated that the most satisfactory treatment of caisson disease is recompression at a pressure which will relieve all symptoms, plus one atmosphere of pressure. The patient is best kept for 30 minutes at the highest pressure, 75 lb. which is equivalent to a depth of 165 feet, before beginning to decompress. They decompressed the patient at the rate of 25 feet per minute until the pressure was equivalent to 60 feet. Oxygen inhalation was then begun and continued for 1½ hours during which the patient was gradually decompressed to normal. Yarbrough and Behnke successfully treated 50 cases of helium and oxygen 'bends' by this method. If this treatment failed, they returned the patient to the pressure at which relief of the symptoms occurred. This was usually low, about 66 feet, and he was kept at this pressure for from 12 to 24 hours and then gradually decompressed.

Yarbrough, O. D., and Behnke, A. R. (1939) *J. industr. Hyg.*, **21**, 213.

CANCER

See also Vol. II, p. 737, and Cumulative Supplement, Key No. 212.

Aetiology and Pathology

R. D. Passey stated that experimental cancer was first produced in 1914 by Yamagiwa and Itchikawa applying tar to rabbits' ears. It was later discovered that the active carcinogenic agent was 3:4-benzpyrene, the parent substance of which, 1:2:5:6-dibenzanthracene, is also carcinogenic. The position of the benzene rings in benzanthrane compounds has been found to be of vital importance in determining carcinogenicity. The most active benzanthrane known will produce tumours in 35 days. These benzanthracenes have been found to be closely related to the bile acids and the naturally occurring sex hormone sterols. These substances are all fat-soluble carcinogens, but a water-soluble carcinogen has been synthesized which will produce tumours on subcutaneous injection, and further will render the blood of the animal carcinogenic. A non-irritating substance, styryl 430, which is not related to the benzanthrane carcinogens, has been found to be actively carcinogenic, so that irritation *per se* is apparently not important. The injections of carcinogens in large doses will slow the rate of growth of spontaneous or grafted tumours, and even slow the growth of normal tissue. The way in which carcinogens act on the tissues is not known, however, the action may be remote, as in the case of bladder cancer in aniline dye workers.

Mustard gas has been found to have a remarkable inhibitory effect on tumour formation, if applied to an area treated with carcinogens before the growth has developed. Cantharidin is also inhibitory.

Tumours arising as a result of X-rays and radium are extremely slow in developing, and have therefore been little used in the laboratory. It is well known that excessive exposure to sunlight can induce epithelioma of the skin. The active factor has been shown to be ultra-violet light. Heat and cold have also been known under certain circumstances to induce cancer. It would seem possible that, with both chemical and physical carcinogens, there is an intermediate tissue product.

The experimental 'virus' tumours yield a filtrable carcinogenic 'agent' of an unknown nature. High speed centrifugalization shows that the agent is particulate. Its antigenic properties have been extensively studied. Chemically induced tumours in birds—in which the 'virus' tumours occur spontaneously—do not yield the virus. There is a definite relationship between the virus tumours and infective warts in animals.

The association of schistosomiasis with bladder cancer is, although often recorded, not definitely known to be causal. A cysticercus sarcoma occurs in the liver of rats, but a hereditary susceptibility also is required.

Hereditary liability and resistance to spontaneous cancer in definite sites have been demonstrated in mice. In human beings, there is a statistically significant increase

in cancer among the relatives of cancer patients, and this increase is most marked in the same organs.

L. A. Emge stated that evidence is forthcoming to show that the provocative causes vary with different types of cancer, and probably vary in their specificity in different species. It is pointed out that in mice (in which the highest cancer incidence of the mammalian world is found) indications show that the factor of prime importance is hereditary susceptibility, combined with the presence of oestrogen. This view is supported by the fact that a strain of rats, which normally showed considerable immunity to mammary cancer, and which were given massive doses of aqueous theelin and of theelin in oil showed no malignant changes in the mammary glands, in the genital tract, or in transplanted mammary adenofibromas. Evidence is accruing to prove that the cancer-provoking faculty of the oestrogenic hormones in small laboratory animals is strictly limited by hereditary tendencies.

E. E. Faerber reviews the two conflicting views regarding the cause of cancer, the virus hypothesis and the chemical agent hypothesis, and argues that it might be assumed that the virus is an integral part of the normal energy-producing mechanism of each cell and that, under the influence of carcinogenic agents, it is altered in relation to the metabolism of the cell. It is suggested that this alteration probably affects the central respiratory mechanism of the cell, and it is thought that the particular system affected in malignancy is the oxidase-cytochrome system. It is considered that sex hormones may also act through this system. It is shown that the glycolytic property of the cancer cell is intimately connected with its malignant properties, and that there is an interrelation between glycolysis and respiration. The suggestion is made that a new chemical substance is formed spontaneously from some part of the oxidase-cytochrome (Warburg-Kcilin) system which confers upon the cell the property of malignancy, and support is furnished by the fact that a high glycolytic property of tissues qualifies them for a relatively early liability to cancer. That malignant tumours may be transmitted by cell-free filtrates is due to the presence of the chemical agent above and a tissue specific protein substance. This combination in the opinion of the author is equivalent to the 'virus'.

Hypothesis of Periodicity

The hypothesis of periodicity in cancer and other neoplastic diseases is advanced by J. H. D. Webster and supported by evidence which the author obtained in the investigation of 450 patients who showed a definite periodicity of 33 weeks (8 lunar months) with, in some cases, half periods of 4 lunar months. The variability has been one of plus or minus 3 weeks. The types included in this study were cancer of the breast, mouth, bladder, thyroid, testis, sarcoma, leukaemia, lymphadenoma, lymphoblastoma, and benign neoplasms. Periodicity was found to be valid in 96 per cent of the patients under review, the evidence being both clinical and radiological, apart from cases of very chronic tumours or tumours in inaccessible sites. The author considered that the virus theory was strongly supported by these findings, and that where a recurrence did not become obvious at the expected time the presence of a quiescent virus was suggested. This would germinate when its own cycle of activity corresponded with a lowered resistance or hormonal stimulus in the host. Growth and transmissibility were found to be more vigorous in the early or spring months of the year, thus showing a seasonal periodicity. By calculating the date of recurrence the author believes that much may be accomplished by prophylactic radiation of sufficient dosage to a wide enough area. It was found also that, in advanced cases, death occurred at or near the maximum peak period.

Emge, L. A. (1939) *Surg. Gynec. Obstet.*, **68**, 472.

Faerber, E. E. (1939) *S. Afr. med. J.*, **13**, 239.

Passsey, R. D. (1939) *J. R. Inst. publ. Hlth*, **2**, 16.

Webster, J. H. D. (1938) *Brit. J. Surg.*, **26**, 113.

Treatment

In a review of 194 cases of carcinoma in various parts of the body, the treatment of which dated back over 2 or more years, E. v. Schubert shows that advanced carcinoma cannot be cured by super-voltage therapy. The results in 105 cases of carcinoma of the cervix, however, were worthy of attention. Of the 105 cases, 92 were in Stages III or IV; of the 19 cases in Stage IV none was cured, but 14 out of the 73 in Stage III are alive and well after 2 or more years. Results were also good in the case of vaginal carcinoma. The fact that, with other lesions, only occasional good results were achieved, was due to the advanced state of the disease when

patients were first seen. The results of prophylactic post-operative irradiation of carcinoma of the cervix were very promising. It was found that super-voltage therapy with massive irradiation within the space of a few days gave better results than serial irradiation. Furthermore, it was shown above all that a lower dosage gave better results than a higher one. The dose should, therefore, not exceed 2,000 *r* given within 2 days and through 2 large fields. This can hardly injure the skin, so that under certain circumstances such a dose might be repeated after a few months. For the destruction of the primary tumour in the case of carcinoma of the cervix, local radium treatment seems definitely indicated. It has been demonstrated that the smallest effective dose is the best and that a dose which is too high increases the number of recurrences and favours general metastasis of the tumour. Super-voltage therapy is not suitable for incurable cases, in whom it does not help and only exhausts the patient unnecessarily. This work also proves that the fate of carcinoma patients depends upon early diagnosis.

Schubert, E. v. (1938) *J. Radiol.*, **31**, 142.

CATARACT

See also Vol. III, p. 1.

Aetiology

For the relation between dinitrophenol medication and cataract formation, see p. 188

Treatment

Vitamin C

S. M. Bouton noted clouding of the optic media of many patients between the ages of 41 and 73 leading to impairment of vision. In some cases the process accompanied early cataract, in others it preceded senile cataract, and in others it occurred alone. Investigation of the excretion and blood-values of vitamin C in these patients showed it to be deficient and treatment with ascorbic acid favourably influenced the condition, provided the lens was not cataractous. If there was no improvement after a daily dose of ascorbic acid for 2 weeks, it was found useless to continue the treatment.

Surgery

W. W. Gailey discussed some problems which are encountered in cataract surgery. Before beginning operation it should be ascertained that the patient has perception of light in the eye and that the general condition is good. If the blood pressure is high, measures should be instituted to reduce it as it may lead to haemorrhage. The lacrimal sac, if infected, should be excised. Gailey no longer takes conjunctival cultures before operation, nor does he scrub the skin vigorously. Measures should be taken to control cough and nervousness. He believes that all cases are suitable for intracapsular extraction except those complicated by high blood pressure or extreme excitability of the patient, asthmatic patients with a chronic cough, those having enlarged prostates, with rigid pupils, high myopia, glaucoma, or Morgagnian cataracts.

Before operation a 4 per cent solution of cocaine hydrochloride is instilled into the eye every 2 minutes for 6 instillations. This is followed by retrobulbar anaesthesia. Adrenaline is instilled just before making the section, but it is thought that this drug may favour secondary haemorrhage. The patient is given some sedative before operation, but is not purged. The eye is fixed at 6 o'clock, and the section made. A good conjunctival flap is important for healing, a 2 mm. flap laterally and 3 to 4 mm. flap apically being ideal. If blood appears in the anterior chamber, it can be washed away later, and is of no importance. If vitreous presents at this stage, the condition is very serious. The speculum should be carefully removed, conjunctival sutures applied, and the lens extracted carefully with a wire loop. Gailey advocates a small peripheral iridectomy before the lens is extracted. Should the iris prolapse, better results are obtained if its repair is delayed until the eye is white. The capsule forceps should be used with care and should grasp the lens low down. After operation the anterior chamber may not refill. Removal of the bandage may remedy this.

Stress and strain of all kinds should be avoided to prevent post-operative haemor-

rhage. This usually occurs on the fifth day, and, although such measures as diathermy and dionin may be instituted to aid its absorption, it is doubtful whether they affect the rate of absorption. The eye should be dressed daily, and the unoperated eye covered for 24 hours at most. This last measure reduces the incidence of post-operative mania. If pain occurs the eye should be inspected and, if nothing is found to be wrong, some sedative given for its relief. The pupil should be kept dilated with atropine. If post-operative detachment of the retina occurs, the prognosis as regards cure is hopeless. Post-operative glaucoma should be treated with cyclo-dialysis. Gailey sends his patients home on the tenth day, and waits until the eye is white before needling the capsule.

Bouton, S. M. (1939) *Arch. intern. Med.*, **63**, 930.

Gailey, W. W. (1938) *Amer. J. Ophthalm.*, **21**, 855.

CEREBELLAR DISEASES

See also Vol. III, p. 21, and p. 94 of this volume.

Cerebellar Form of Guillain-Barré's Syndrome

Guillain *et al.* described a syndrome not observed before, its main symptom was polyneuritis combined with albumin-cytological dissociation in the cerebro-spinal fluid, the albumin being much increased but the number of cells normal or only slightly increased. The prognosis was good, as also appears from the relatively small number of similar cases described below. J. O. Trelles and C. J. V. Bernales examined 2 cases of this syndrome, in both of which cerebellar signs were marked. In the first case the left labyrinth was affected; other signs on the left side were deafness, facial paralysis, paralysis of the superior oblique and internal rectus muscles, paralysis of the palatine velum, anaesthesia in the sphere of the 5th nerve, cerebellar signs—hypotonia, ataxy, and adiadochokinesis, and diminished sensibility and tendon-reflexes. On the right side only the superior oblique was affected. Papilloedema was observed at the first examination, as well as headache, photophobia, and vomiting. In the cerebrospinal fluid albumin was increased, but the number of cells was normal. The patient made a complete recovery. Cerebellar signs were also observed in another patient who began to recover 2 months after the onset and was almost completely well 10 months after the trouble started. Cerebellar signs observed in these 2 cases demonstrated that the toxic cause producing this affection may damage not only the peripheral nerves and their roots but also central parts of the nervous system.

Trelles, J. O., and Bernales, C. J. V. (1939) *Rev. Neuro-psiquiat.*, **2**, 62.

Spino-Ponto-Cerebellar Atrophy

E. Welte examined clinically and microscopically 4 cases of atrophy of the pons and inferior olives. The atrophy affected the neurons of the basilar part of the pons and inferior olives on both sides. The arcuate nucleus and the nucleus pterygoideus were also atrophied. The atrophy started in the periphery of the neurons, i.e. in the central part of the cerebellum. A certain degree of atrophy in the cerebellar cortex was a result of secondary degeneration. Numerous intermediate links justify the combination of all forms of 'cerebellar atrophy', including Friedreich's ataxy, atrophy of systems of the basilar part of the pons and inferior olives, primary atrophy of the cerebellar cortex, and atrophy of systems of the corpus dentatum and superior cerebellar peduncles, under the name 'spino-ponto-cerebellar atrophies'. The fourth case described in this paper showed atrophy of the corpus dentatum and superior peduncles of the cerebellum. The spinal segments of the peripheral motor neurons and spinal tracts were atrophic, as observed in Friedreich's ataxy; mild atrophy was also observed in the basilar systems of the pons and in the inferior olives.

Welte, E. (1939) *Arch. Psychiat. Neurol.*, **109**, 649.

CEREBRAL DIPLEGIA

See also Vol. III, p. 27.

Aetiology

According to C. H. Heyman the causes of congenital spastic paraplegia (Little's

disease) effective before conception are syphilis and a neuropathic heredity. During pregnancy the toxæmias and primary neurogenic degeneration have a considerably adverse influence.

Heyman, C. H. (1938) *J. Amer. med. Ass.*, **111**, 493.

Clinical Picture

R. L. Jenkins and M. Lesser investigated the differences in motor stability and in the ability to adapt themselves to a sudden auditory stimulus between normal children and children with spastic paralysis. The paralytic children were classified as hemiplegic, paraplegic, and quadriplegic, and were grouped according to the cause of the paralysis, namely birth injury, injury after birth, encephalitis, hydrocephalus, tumour of the brain, and unknown causes. All the paralytic children in the series were less able to adjust themselves to startling auditory stimuli than were the normal children. The paralysed extremities practically always reacted to the stimuli by movement. In hemiplegia the affected hand was less steady both with and without the stimulus and in quadriplegia the reaction was still more intense. Children with athetosis reacted severely and unsteadily. The authors considered that these reactions are explained by a diminished cerebral inhibition of the reflex motor response to a sudden auditory stimulus in a child with cerebral paralysis.

Jenkins, R. L., and Lesser, M. (1938) *Amer. J. Dis. Child.*, **56**, 266.

CEREBROSPINAL FEVER

See also Vol. III, p 39, Cumulative Supplement, Key No. 223; and p 125 of this volume.

Treatment

Serum Therapy

H. J. A. Lober states that he has reduced the mortality in meningococcal meningitis to 10 per cent by serum therapy. In each case taken into hospital with signs of meningitis, lumbar puncture was performed immediately. The whole cerebrospinal fluid was removed, if it was not quite clear. Twenty c.cm. of anti-meningococcus serum (10 c.cm. in infants) at body temperature was injected immediately after removal of the cerebrospinal fluid. If only 20 c.cm. of cerebrospinal fluid could be removed, 10 c.cm. of serum only were injected in order to prevent increase of pressure, and 10 c.cm. of serum were given intramuscularly or intravenously in such a case. If signs of meningococcal meningitis were apparent on examination of the cerebrospinal fluid, lumbar puncture was performed on each following day; the whole cerebrospinal fluid was removed and 20 c.cm. of serum injected. This treatment was continued as long as bacilli were found in the cerebrospinal fluid. Daily injection of 100 c.cm. of serum was given, in one case for 20 days. Serum injection was resumed, if bacilli were observed again. Lumbar puncture must be continued while the cells in the cerebrospinal fluid are above 50 per c.cm. The quantity of serum varies according to the case. Of 22 cases 17 were cured in this way.

N. W. Bolduan recommended for the first few days of meningococcal meningitis intraspinal injections of the most potent anti-meningococcus serum available, at intervals of 12 hours. Better results were obtained than if intervals between injections were 24 hours. The case fatality rate was lower, the hospital stay shortened, and the total amount of serum used totalled an average of 165 c.cm. which was only slightly more than with the 24-hour method. A lowered death-rate in New York is attributed to this method of treatment in combination with earlier diagnosis and increased potency of the serum used.

M & B 693

R. B. Usher Somers reviews 143 cases of cerebrospinal fever in the Sudan which were treated under field conditions by M & B 693. Three methods of administering the drug were devised. (i) Varying amounts of a suspension of 0.5 g. of M & B 693 in 40 c.cm. of distilled water were given intrathecally and intramuscularly simultaneously. Treatments were carried out on consecutive days, but in some cases only one treatment was given. In no case did the total dose exceed 1.2 g. Of 18 patients in this group 7 died. (ii) A watery suspension of M & B 693 (0.5 g. in 80 c.cm. of water) was administered intrathecally (3 to 10 c.cm.) and intraperitoneally (25 to

80 c.cm.). The maximal total dose was also 1.2 g. Of 56 patients so treated, 4 died. (iii) A watery suspension of M & B 693 was injected intrathecally (dosage as in the first group) and an oily suspension (0.5 g. in 2.5 c.cm.) intramuscularly; the intramuscular dosage was 1 to 5 c.cm. The average total of M & B 693 for this group was 1 g. and the maximum never exceeded 3 g. Of 66 patients, 3 died. The use of this therapy, more particularly in its two latter forms, reduced the mortality of cerebrospinal fever from 68–80 per cent during the previous 5 years in the same locality to 10 per cent.

W. H. Osborn supplies further evidence of the efficacy of the treatment of meningococcal meningitis by M & B 693 in an account of the treatment of 3 cases of cerebrospinal meningitis occurring in men of 49 and 44 and in a woman of 33. An average dose of 29 g. of M & B 693 was given in each case, and lumbar puncture was carried out daily until the sixth or seventh day, when the appearance and pressure level of the cerebrospinal fluid had returned to normal.

F. G. Hobson and D. H. G. MacQuaide investigated the action of M & B 693 in 6 cases of meningococcal meningitis, all of which recovered. In 2 cases a concentration of no more than 3 mg. per 100 c.cm. in the cerebrospinal fluid produced an effective bacteriostasis. The passage of the drug from the gastro-intestinal tract into the blood was rapid, but the rate of passage was related to the state of the gastro-intestinal tract. The passage of the drug from the blood to the cerebrospinal fluid was also rapid and the concentration of the drug in the cerebrospinal fluid was approximately half of that in the blood-stream. Cyanosis appeared in one case but disappeared when the drug was withheld for one day. Nausea and vomiting did not occur. Examination of the urine showed that half the drug was excreted unchanged, and half in the form of an acetyl derivative.

Uleron

Because uleron is so effective in gonorrhoea, and because gonococci and meningococci are much alike, K. H. Schaefer employed this drug in 17 children of ages ranging from 2½ months to 3 years suffering from cerebrospinal fever. The uleron was given orally for 4 days; after an interval of 3 days, the regime was repeated as often as necessary. The total dosage in the patients who were cured ranged from 18 g. (6 months old) during 54 days to 63 g. (2 years old) during 83 days. Ten children died, during a period of from 2 days to 65 days after admission. In addition to the uleron treatment lumbar puncture (in one case, which was eventually cured, 25 times), and in 3 cases a blood transfusion was made. The author was under the impression that the uleron not only failed to relieve the symptoms but aggravated them at least in one case, and concluded that the drug has definitely no favourable influence upon infantile epidemic meningitis.

On the other hand, H. Oetken successfully treated with uleron 2 very severe cases of meningococcal meningitis, one in a man aged 18 and the other in a woman aged 35, after serum injections had failed to improve the condition. The dose used was 6 tablets of uleron daily for 4 days in one case, and 6 days in the other. This course was repeated after an interval of 10 days in one case; the other patient had 5 courses of uleron, separated by intervals of 6 days. During the intervals, glucose and hexamine were injected intravenously. Complete cure resulted. This does not as a rule occur in such severe conditions with other methods of treatment. The author is of the opinion that the good effect of uleron is due to the biological relation between meningococci and gonococci.

Serum Therapy and Sulphonamide Drugs

A. A. Koltypin summarizes his cases, during the last 12 years, comprising more than 322 children suffering from cerebrospinal fever, and his treatment both with and without anti-meningococcal serum. The commonest type of reaction following the administration of the serum was serum sickness. Ependymitis often followed, generally ending in death. He finds that the serum treatment favourably influenced the course of the disease. He devotes the paper chiefly to the newer method of treatment of meningococcal meningitis by the administration of streptocide (sulphanilamide), simultaneously with antimeningococcal serum, and the results of its administration to 10 children. All had a severe form of meningitis and their ages ranged from 3 months to 8 years. All these 10 children recovered; one had ependymitis. Three other children, aged 4 months, 8 months, and 6 years respectively, all with complications, either influenza, pneumonia, diphtheria, arthritis, or mastoiditis, also recovered following the streptocide treatment. The oldest was abnormal

mentally and later became deaf. The doses given were from 0.4 to 0.6 g. daily for 10 days.

W. J. Roche and C. J. McSweeney published the results obtained from the treatment of cerebrospinal meningitis by M & B 693. Eleven cases in sequence were treated by this drug, by intravenous and intraperitoneal serum therapy, and by daily spinal drainage until the cerebrospinal fluid was clear and sterile. Ten of the 11 patients recovered, the eleventh dying from respiratory failure, a case mortality of 9.1 per cent. Of the 11, 6 were under one year and among these, as 5 recovered, the mortality for the age group was 11.66 per cent. This was contrasted with a figure of 78 per cent in a series of 46 cases under 1 year treated by intrathecal serum alone in the same institution. Hydrocephalus, which had been a sequel to posterior basic meningitis in the previous series, was absent following the new form of treatment. The dosage of M & B 693 varied considerably.

L. Revadeau *et al.* reported the successful treatment of meningococcal septicaemia with fulminant purpura and purulent meningitis by the combined administration of sulphanilamide and anti-meningococcus serum in a male infant, 9 months old. In contrast, a fatal case in a male infant, 5 months old, treated by sulphanilamide only was described.

Meningeal 'Washing'

O. Künzel treated 9 cases of cerebrospinal fever by washing the meninges. None of the patients died. Occipital and lumbar puncture was performed as soon as the patients arrived in hospital and a large amount of cerebrospinal fluid was removed. Sterile isotonic saline was injected at the occipital puncture and flowed out at the lumbar puncture; 300 to 500 c.cm. of fluid were injected daily. In some cases the fluid used in washing did not become quite clear at the first washing. The majority of patients started to feel better during the injection. The author suggests that this treatment should be combined with serum therapy and uleron, although nothing definite was observed with regard to the value of these 2 treatments.

Bolduan, N. W. (1938) *J. Pediat.*, **13**, 357.

Hobson, F. G., and MacQuaide, D. H. G. (1938) *Lancet*, **2**, 1213.

Koltypin, A. A. (1939) *Vrach. Dveto*, **21**, 10.

Kunzel, O. (1939) *Dtsch. med. Wschr.*, **65**, 792.

Löber, H. J. A. (1939) *Munch. med. Wschr.*, **86**, 918.

Oetken, H. (1938) *Dtsch. med. Wschr.*, **64**, 1683.

Osborn, W. H. (1939) *Brit. med. J.*, **1**, 1281.

Revadeau, L., Chabrun, J., and Dufour (1939) *Bull. Soc. Pédiat. Paris*, **37**, 163.

Roche, W. J., and McSweeney, C. J. (1939) *Brit. med. J.*, **1**, 1278.

Schaefer, K. H. (1939) *Dtsch. med. Wschr.*, **65**, 165.

Somers, R. B. U. (1939) *Lancet*, **1**, 921.

CEREBROSPINAL FLUID

See also Vol. III, p. 52.

Lumbar Puncture

Indications

According to H. H. Hepburn the dangers of spinal puncture in the presence of increased intracranial pressure have been overstated and, as a result of supposedly authoritative warnings, this valuable diagnostic procedure has in some cases been withheld or delayed, with detriment to the patient. The only absolute contra-indication to spinal puncture is the probable presence of an intradural abscess, including cerebral abscess. As relative contra-indications, he mentions the probability of brain tumour in the posterior fossa and of haemorrhage from an intracranial aneurysm, but he does not consider either of these an absolute contra-indication provided due caution is observed. Even when tumour in the posterior fossa is suspected the author believes 2 or 3 c.cm. of cerebrospinal fluid may be removed slowly without great danger. This quantity should be sufficient for the differential cell count, Wassermann test, and gold curve. In the absence of papilloedema and of any appreciable fall in the spinal pressure, 6 or 8 c.cm. may be removed for complete examination. An initial high pressure with a rapid fall should be recognized as a

danger signal. A manometer should be used during the procedure, not once but repeatedly when a high initial pressure is found. In the hospital records for the last 6 years there was one case only of a cerebral tumour which proved fatal on the same day that spinal puncture was performed.

Hepburn, H. H. (1938) *Canad. med. Ass. J.*, **39**, 449.

Osmotherapy

M. Ernst summarized the present outlook on the intravenous injection of hypertonic solutions in the therapy of increased intracranial pressure, a method which was established about ten years ago. He recollected the results of animal experiments which showed that the injection of hypotonic solutions into the blood stream increased cerebral pressure, whereas the injection of hypertonic solutions, such as glucose and sodium chloride, decreased cerebral pressure. Experiments also proved that the same results were obtained after rectal infusion of the fluids, or on intra-abdominal administration.

Osmotherapy must be understood in order to obtain good results, and therefore it must be remembered that cases promise success only when intracranial pressure is due to a sudden accumulation of fluid. The production of cerebrospinal fluid is decreased on injection. Hydrocephalus, tumours of the brain, large apoplectic foci, and epilepsy are all unsuitable for osmotherapy. On the other hand, if these conditions are accompanied by an acute increase of cerebral pressure, osmotherapy will reduce the newly increased pressure to the old level. Osmotherapy is most beneficial in the course of commotio cerebri. In the first 24 hours of a cranial injury osmotherapy should never be tried. Post-commotional symptoms react very quickly to the injection of hypertonic solutions. The author recommended 30 per cent glucose as superior to hypertonic saline.

Ernst, M. (1939) *Munch. med. Wschr.*, **86**, 773.

CERVICAL RIB

See also Vol. III, p. 75.

Incidence and Clinical Picture

Delay in the onset of symptoms due to cervical rib until the second or third decades of life has been, D. B. Davis and J. C. King agree, attributed to the fact that ossification and growth of the cervical rib are not complete until the twenty-fifth year and descent of the shoulder girdle is not generally complete until the twentieth year; should any or all of the stages of development occur prematurely, symptoms may arise at an early age. The authors reported 3 such cases in children, and examined 1,000 radiographs of the chest made on children under 13 years, 12 of which showed the presence of cervical ribs. Oblique radiographs of the neck and upper part of the chest taken with the rays directed upwards, laterally, and posteriorly through the seventh cervical vertebra demonstrate the proportions of the rib. In children under 5 years a centre of ossification which is a potential precursor of a cervical rib will show as a separate piece of bone adjacent to the transverse process of the seventh cervical vertebra.

Davis, D. B., and King J. C. (1938) *Amer. J. Dis. Child.*, **56**, 744.

CHANCROID

See also Vol. III, p. 97, Cumulative Supplement, Key No. 227; and p. 155 of this volume.

Treatment

Sulphonamide drugs

H. Järnecke found that, in a patient with gonorrhoea and chancroid treated with uleron, both the gonorrhoea and the chancroid disappeared. The author then tried systematic treatment of chancroid with uleron. He treated altogether 15 cases, some of them with very extensive ulcerations. There were no recurrences, and the scars seemed to be far less visible than usual. The dosage of uleron in the first cases treated was 0.5 g. 7 times daily for 7 days, i.e. 24.5 g. Later the dosage was reduced to 0.5 g.

5 times daily for 5 days, i.e. 12.5 g.; eventually it was changed to 0.5 g. 6 times daily for 3 days, followed by an interval of 5 to 6 days, and then 0.5 g. 6 times daily for 3 days, this treatment in 2 'bouts' seems to be most effective. Treatment of chancroid with prontosil was not very successful; the ulcer was influenced, but not to the same extent as with uleron.

Circumcision

J. E. Rauschkilb adds 247 additional cases to the already existing list of cases of chancre treated by circumcision. Circumcision, according to the author, should be recommended whenever it is indicated as prophylaxis against bubo, to relieve phimosis and paraphimosis, and to render inaccessible lesions visible for critical diagnostic study and efficient treatment. A block anaesthetic is used—a 2 per cent solution of procaine hydrochloride without adrenaline after an injection of morphine $\frac{1}{4}$ grain and scopolamine $\frac{1}{160}$ grain—and the prepuce amputated by the guillotine method. The wound is dusted with iodoform powder, a suspensory bandage applied and the patient kept in bed 3 to 5 days, without any dressing, under a cradle continuously heated with a carbon filament lamp. Hot freshly prepared potassium permanganate soaks are employed for 10 minutes, 4 times daily. Among the 247 patients circumcised, no bubo was found after operation, if it had not existed preoperatively.

Jarnecke, H. (1938) *Med. Welt*, **12**, 1872.

Rauschkilb, J. E. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 319.

CHILD HEALTH AND WELFARE

See also Vol. III, p. 132, and p. 37 of this volume.

Neonatal Serum Calcium

B. S. Denzer *et al.* studied the serum calcium values in the first 10 days of extra-uterine life. At birth the blood in the umbilical cord showed values 1 to 3 mg. per 100 c cm. higher than the maternal blood. In the first 4 days of extra-uterine life there is a deep depression in the calcium level of about 1.21 mg. Thereafter the curve gradually rises, though not to the initial level. The fall is uninfluenced by birth-weight, the degree of neonatal weight loss, or the type of feeding. It is unrelated to serum protein, which is constant throughout the period. It is also unrelated to the blood phosphorus. The cause of this depression is therefore unknown. The fall in serum calcium in the series studied never reached tetanic levels. The high calcium level at birth supplies a margin of safety.

Denzer, B. S., Reiner, M., and Weiner, S. B. (1939) *Amer. J. Dis. Child.*, **57**, 809.

Neonatal Diarrhoea

Prevention

In view of the spread of fatal diarrhoea of the new-born in the United States, M. L. Spivek questioned if present-day hospital nursery practices are beyond reproach. He considered that, as correction is very difficult, dispersion of the nursery is in all probability the simplest solution. As alternatives he offered (i) cubicle units each completely equipped; (ii) nurseries of 3 or 4 beds closely associated with a similar number of maternal beds; (iii) that new-born infants should be housed in rooms adjacent to the mother's or in the mother's room; (iv) hospital delivery and discharge within 48 hours; and (v) home delivery.

Spivek, M. L. (1938) *J. Amer. med. Ass.*, **111**, 1065.

CHOREA

See also Vol. III, p. 204, and Cumulative Supplement, Key No. 237.

Aetiology

S. J. Usher analysed the incidence of heart disease in a group of children presenting a history of. (i) true chorea, that is one or more attacks of chorea uncomplicated

by any other rheumatic manifestations; (ii) mixed chorea, those which present histories of chorea, with other manifestations of rheumatism. Of 56 pure choreas, 27 per cent had definite cardiac involvement on admission to hospital, but, omitting those cases with infected tonsils and repeated upper respiratory infections, only 14 per cent were associated with endocarditis. In the group of 49 mixed choreas 65 per cent showed a considerable degree of enlargement and of these 22 per cent showed heart disease. Four case reports are given of active choreas. None of the patients had any history of previous rheumatism or heart disease on admission. Three experienced joint pains and the fourth a severe upper respiratory infection. They all developed heart disease.

In analysing the causal factors in both chorea and rheumatism it was found that the age incidence and economic level were similar. In both conditions the child is endowed with a nervous constitution, but there is nothing to suggest that chorea is an infection from the point of view of its clinical course, temperature, pulse, or blood count.

The author urged that, in treating the choreic child, the basic nervous constitution and the susceptibility to psychic trauma should not be neglected. The condition, he stressed, had too long been regarded as merely a major rheumatic manifestation

Usher, S. J. (1938) *Canad. med. Ass. J.*, **39**, 565.

CHOREA, HUNTINGTON'S

See also Vol. III, p. 211.

Differential Diagnosis

Senile Chorea

R. Pauly observed that generalized chronic chorea was more rarely a result of heredo-degeneration (Huntington's chorea) than it was supposed to be, and that cases of non-hereditary chorea were more common. The chorea in such cases was characteristically mild. Mental signs may be present or absent. Syphilis was only exceptionally an aetiological factor, arteriosclerosis was sometimes the cause. Microscopical changes were similar to those in Huntington's chorea, but absence of affection in the frontal lobe was observed in some cases. In a case of hemichorea the change seen in chorea of younger persons was observed, affection of the putamen, nucleus caudatus, nucleus Luysii, and cerebellar peduncles.

A true acute chorea may arise after the age of 60 years. If these patients had suffered at an early age from Sydenham's chorea or arthritis the affection might be a relapse. Primary senile chorea was observed in female patients more often than in male. Senile chorea may be true Sydenham's chorea; it may, however, be a result of infection by a neurotropic virus comparable to or identical with the virus of epidemic encephalitis. Microscopical examination shows a lesion in the same part of the brain as in a case affected by chorea arising at an earlier age. The difference maintained between acute infective chorea and degenerative chronic chorea (Huntington) is justified. But certain cases of chronic non-hereditary chorea may result from infection.

Pauly, R. (1938) *Encéphale*, **33**, 239.

CLIMACTERIC AND ITS DISORDERS

See also Vol. III, p. 228, and Cumulative Supplement, Key Nos. 242 and 243.

In the Female

Endocrine Factors

B. P. Watson *et al.* describe the loss of response of the human ovary to gonadotrophic stimulation with age. There is a slight response in the fourth decade of life and a complete absence of response in the fifth decade and after. One ovary may cease to function before the other. The authors conclude that the menopause is due to this loss of response.

Treatment

Oestrogen.—L. F. Hawkinson treated 1,000 patients suffering from the menopausal syndrome with oestrogenic preparations. In those in whom the menopause was artificially induced the symptoms were severe, including nervous, vascular, glandular, and digestive upsets. The diagnosis in this series was made from the signs and symptoms and in doubtful cases from the examination of the vaginal smear. The patients were divided into 3 groups; one received oestrogenic preparations hypodermically, the second orally, and the third by a combination of the 2 routes. In the first group it was found that 10,000 I.U. every 3 or 4 days, for about 12 injections, was the average amount necessary to control symptoms. Oral dosage required up to 6,000 I.U. daily for between 15 and 60 days. All these methods gave good results provided the dose was high enough, and it was found necessary to continue the treatment until all the symptoms had subsided and the patient remained symptom-free after treatment had been suspended.

Follicular hormone.—B. C. Murless reported the results obtained in the treatment of 51 patients who had undergone an artificial menopause following radium therapy, when given small doses of ovarian follicular hormone. These 51 women were treated for periods ranging up to 6 months, the therapy commencing between 8 and 12 weeks after the menopause. Each tablet contained 0.025 mg. of oestradiol, the largest daily dose being 8 tablets. The average dosage was 4 tablets daily, which was increased to 6 or 8 according to the result at the end of a fortnight. The increase was maintained for 4 weeks, and, if the 'flushes' were sufficiently controlled, the tablets were reduced to 6, then 4, and finally 2. Improvement was generally maintained and a reversion to large doses was unnecessary. Controls given merely tablets of lactose experienced no reduction in the number of 'flushes' in 24 hours. The final results were as follows: in 11 cases a complete cure resulted after an average period of treatment lasting 4 weeks; in only 5 cases did treatment fail to reduce the number of 'flushes' and even in 4 of these their severity was diminished. The remainder showed varying degrees of improvement. Symptoms did not return within the ensuing 6 months.

Hawkinson, L. F. (1938) *J. Amer. med. Ass.*, **111**, 390.

Murless, B. C. (1939) *Lancet*, **1**, 1205.

Watson, B. P., Smith, P. F., and Kurzrok, R. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 562.

CLIMATE IN THE TREATMENT OF DISEASE

See also Vol. III, p. 235

Mountain Sickness

N. Sirotnin during the ascent of Mount Elbrus (18,525 feet) found a noticeable fall in the alkaline reserve in cases of mountain sickness. He also found that the symptoms of mountain sickness disappeared as the number of erythrocytes increased. He made experiments on persons and mice in a special closed chamber as well as during the Elbrus climb. A climber A who received 15 g. of citric acid and 200 g. of sugar daily, felt much better than the climber B who received 15 g. of sodium bicarbonate with the same quantity of sugar. Mice in the chamber with the rarefied air were better after blood-letting followed by a blood transfusion. The mice under diminished pressure in the chamber and 20 mice taken to the mountain showed greater increase in erythrocytes when given injections of arsenicals than the control mice without injections. Observations on a man in the chamber showed that, on lowering the atmospheric pressure, the number of erythrocytes and percentage of haemoglobin increased when iron and arsenic were taken. This same result was obtained on 3 men during the Mount Elbrus climb. The author is of the opinion that arsenic should be used as a prophylactic for mountain sickness and for the treatment of anaemia.

Sirotnin, N. (1938) *Medichny J.*, **8**, 327.

Climatic and Socio-Economic Factors in Relation to Disease

L. P. Herrington and I. M. Moriyama reviewed the climatic and social factors in disease in relation to mortality, basing their study upon such diseases as diabetes

mellitus, toxic goitre, Addison's disease, leukaemia, and pernicious anaemia. The geographical distribution of mortality in the United States, taken over a 9-year period, lends statistical support to the nosological grouping of these diseases as metabolic disorders. There is a high average inter-correlation among these 5 causes of death, and a consistent general pattern of relationship between the individual causes and the majority of the climatic and socio-economic variables. The socio-economic factors, in the case of diabetes mellitus, are of greater importance and reflect the frequently observed relation between urban prosperity and the incidence of that disease. A significant relation in which the death-rate from diabetes mellitus is increased with a lowering of normal temperature and increased wind movement reflects the climatic contribution. Pernicious anaemia and leukaemia show a division of influence between climatic and socio-economic factors, in which the latter, as in diabetes mellitus, are much more important. Rates tend to rise, however, with prosperous rural conditions in contrast to the predominantly urban associations of diabetes. The minor climatic associations of pernicious anaemia and leukaemia indicate increased rates for pernicious anaemia in cold and climatically unstable areas, and for leukaemia in areas of relatively stable cold. No conservative interpretation appears available for either of these findings. The independent climatic association with toxic goitre is the largest climatic association in what the authors term 'the metabolic panel', and this, it is considered, indicates high rates in cold and unstable climates. Addison's disease has minimal associations with the climatic and socio-economic variables considered. It is in agreement with other members of the 'katabolic panel' in demonstrating higher rates in the colder regions. A larger statistical experience would be desirable with reference to this cause.

In a further study these authors showed that the States with the highest death-rates from diseases of the circulatory system are chiefly those in the north-eastern section of the United States, whereas the highest mortality-rates for cerebral haemorrhage and chronic nephritis are, with one exception, confined to the south. In considering the factors responsible for these wide variations, the authors have studied the associations between each cause and 11 climatic and 11 socio-economic factors. In the incidence of circulatory diseases, the climatic group of factors appeared to play a real though relatively unimportant part. Cold and stable climates gave higher rates. Socio-economic factors, such as the degree of urbanization, the relative *per capita* income, and the proportion of negroes, had a much more pronounced effect. In the highly urbanized and prosperous area, mortality-rates for diseases of the circulatory system tend to vary in direct proportion with the degree of urbanization and prosperity. In rural and less prosperous states this influence was less prominent and high mortality-rates are here closely associated with the percentage of negroes in the population. Angina pectoris was the only disease which was predominantly affected by climatic factors independent of socio-economic influences. Cerebral haemorrhage mortality appeared to be associated more with precipitation rate than with any other climatic factor. The mortality-rates of chronic nephritis were higher in regions of damp heat and lower in regions of greatest climatic stimulation. These results appear to throw doubt on the conclusion of Mills (1932) that 'a whipping-up of the activity of the glands of internal secretion . . . seems to answer the question as to how weather fluctuation affects the human body'. The authors' final conclusion is that the climatic factors found by competent statistical analysis to be actually associated with mortality are related to a cold and damp climate rather than to a stormy variable one.

Herrington, L. P., and Moriyama, I. M. (1938) *Amer. J. Hyg.*, **28**, 396.

Moriyama, I. M., and Herrington, L. P. (1938) *Amer. J. Hyg.*, **28**, 423.

COCYX DISEASES

See also Vol. III, p. 258.

Pilonidal Cyst

Treatment

Sclerotherapy.—A successful treatment of pilonidal cyst by the use of a sclerosing solution is described by H. I. Bigeleisen. The sinus openings were first probed to find their direction and extent, after which modified Carnoy's solution was injected, a blunt needle being used for the purpose. At the next treatment anaesthesia was obtained by inserting 2 per cent percaine solution on a fine cotton-tipped probe.

Curettage was then performed, using either a fine curette or a long needle the tip of which had been burred over. The sclerosing solution (fuming nitric acid) was next applied by means of a probe which was inserted and then rotated to ensure that the entire surface was treated. The patients experienced no pain. The treatment was repeated every 2 to 4 weeks until complete obliteration took place. In 3 cases no recurrence was found by the end of a year.

Bigeleisen, H. I. (1939) *Amer. J. Surg.*, **44**, 622.

COELIAC DISEASE

See also Vol III, p 262, and Cumulative Supplement, Key No. 247.

Aetiology

Causation of the Low Blood-Sugar Curve

From observations on 12 well-established cases of coeliac disease, including estimations of blood-sugar curves after intravenous injection as well as the oral administration of glucose, T. Crawford found that, whereas after the oral administration of glucose the blood-sugar curve was low, it was normal after the intravenous injection of glucose. It therefore appeared that there was not any abnormality in the intermediate metabolism of carbohydrates and, as all the evidence pointed to the absence of any abnormality in the renal threshold, it was concluded that the low blood-sugar curve was due to defective absorption of glucose from the intestine.

Crawford, T. (1939) *Quart. J. Med.*, N.S. **8**, 251.

Clinical Picture

Thirty-two cases of 'non-tropical sprue', coeliac disease, or 'idiopathic steatorrhoea', occurring in residents in the United States were observed by A. M. Snell. The increasing incidence of this condition in temperate countries was thought to be due rather to more ready diagnosis than to an actual increase in the number of cases. The fact that in non-tropical sprue symptoms not usually associated with the tropical form appeared, was probably the outcome of relatively late diagnosis, as against early recognition in districts where the disease was known to be endemic. Of the 32 cases, 20 presented symptoms diagnostic of tropical sprue. The remaining 12 showed, in addition, various vitamin deficiencies, hypoproteinaemia, and disturbances of calcium metabolism, thus producing a typical picture of idiopathic steatorrhoea. Malabsorption of the various vitamin substances in the digestive tract was a significant feature of non-tropical sprue, the fat soluble substances being the most affected. Symptoms of deficiency of vitamins A and D were shown, and the more recently discovered antihæmorrhagic factor, vitamin K, appeared to be affected. It was suggested that this might have some bearing on the hæmorrhagic diathesis sometimes associated with the fatal termination of this disease. Vitamin B₁ appeared to be absorbed to some extent, but the daily requirements were increased. The appearance of pellagra in 2 patients suggested poor absorption of the anti-pellagra factor. The failure in absorptive function was found to be associated with defective formation of the anti-pernicious-anaemia principle. Hypochromic anaemia, hyperchromic macrocytic anaemia, and the erythroblastic type have all been described in non-tropical sprue. Both the macrocytic anaemia and bowel dysfunction responded to parenteral injections of liver extract. Oral administration was employed successfully in some cases. The results of liver therapy were not so good as in tropical sprue. Tropical and non-tropical sprue originate from a common deficiency condition, but differentiation may be made by some of the symptoms. The large fatty stools typical of tropical sprue are less often found in the non-tropical form. The same applies to aphthous stomatitis and glossitis, whereas in non-tropical sprue, tetany, osteoporosis, oedema, vitamin deficiencies, and degeneration of the spinal cord are more often found than in the tropical form.

A. L. Burgdorf and T. A. Barry reported a case of non-tropical sprue, which demonstrated the typical exacerbations shown when the patient was on a faulty diet, the remissions which occurred with hospitalization, and the association of the condition with ulcers of the stomach and colon, and decrease in height. This patient had not been in the tropics, but had suffered from gastric pain and vomiting for 7 years, for

which a gastro-enterostomy was performed. The symptoms were relieved except for the appearance of diarrhoea. About two and a half years later he was admitted to hospital exhibiting typical sprue symptoms with loss of weight. Anaemia of the pernicious type developed. With rest, cod-liver oil, a low fat and carbohydrate and high protein diet, he improved considerably except for intermittent diarrhoea. He was discharged 7 months later and was put on a general diet, calcium being administered orally. Almost 2 years later he was again admitted to hospital. At this time the blood calcium content was 6 mg. and the serum phosphorus 3.5 mg. per 100 c.cm. Red cells were 2,700,000 per c.mm. and haemoglobin content 65 per cent. He was discharged after 5 months, and after 7 months again readmitted with a history of fainting attacks and spells of unconsciousness. His weight had again decreased. Blood pressure was 70/46 and reflexes hyperactive instead of hypoactive as before. For 5 weeks he improved in hospital and then discharged himself. Seventeen and a half months later he was admitted for the last time, with a history of severe abdominal pain lasting 8 hours. Four days later he died. Examination at necropsy was negative except for physical deformities as the result of bone absorption. There was moderate hypoplasia of the bone marrow, with numerous megakaryocytes. It was considered that the recurrent epigastric distress both before and after the operation was part of the early symptoms of non-tropical sprue, the typical signs developing later.

Burgdorf, A. L., and Barry, T. A. (1939) *J. Amer. med. Ass.*, **112**, 2508.
Snell, A. M. (1939) *Ann. intern. Med.*, **12**, 1632.

Diagnosis

Radiology

J. L. Kantor emphasized 4 radiological signs which, although not invariably present, may, when patent, be considered diagnostic of coeliac disease. The first of these is the 'moulage' sign, a term used to describe a peculiar and characteristic appearance of the jejunum. The valvulae become coarsened and flattened out, and the wall outlines seem softer than normal. There may be dilatation of the small bowel lumen and spasm with sausage formation. In advanced states the bowel bears a resemblance to a tube into which wax has been poured and allowed to harden. In acute cases the emptying time of the whole of the small intestine may be lengthened. The second feature observed radiologically is dilatation of the colon, which results from an accumulation of gas which persists as long as the condition is active, and the patient is on unrestricted carbohydrate diet. A third indication of coeliac disease, as shown by the author, was a failure of the gall-bladder to fill, although in the acute phase in 5 out of 6 cases reviewed no signs of gall-bladder disease could be detected. The sixth case presented a history of jaundice. The obvious bony changes associated with the condition constitute the fourth radiological sign mentioned by the author.

Kantor, J. L. (1939) *Amer. J. Roentgenol.*, **41**, 758.

Treatment

High Protein Banana Diet

The treatment for coeliac disease which is advocated by S. V. Haas consists in a high protein banana diet. The carbohydrate, which is contained in banana, will raise the blood-sugar to a normal figure, not attained by the administration of glucose or laevulose. To secure a specific action, banana must be the only carbohydrate in the diet. Vitamin D concentrate and iron may prove valuable supplementaries. The prognosis on this diet is excellent.

Haas, S. V. (1938) *J. Pediat.*, **13**, 390.

COLDS

See also Vol. III, p. 271.

Aetiology

A. Locke stated that infection, sufficient to produce enlargement of the cervical glands, lowered the resistance to the common cold. Older people presumably have fewer colds than the young because they have fewer foci of low-grade infection. Although the senescent are more liable to pneumonia, they are not more liable

to the common cold. The author also found that fatigue rendered men more susceptible to common cold infection.

Locke, A. (1939) *J. Immunol.*, **36**, 365

Preventive Measures

Ultra-Violet Irradiation

J. B. Sherman described an attempt made at the Bournville Works to estimate the value of 4 current methods of prophylaxis against colds, employed on 1,062 persons, and controlled by 593 others. The 4 methods were: (i) Ultra-violet irradiation, the apparatus used being a pair of Watson carbon-arc lamps. Exposures were given at a distance of 3 feet twice a week, working up to a total exposure of 14 minutes. This was carried on throughout the winter, no ill effects being noted. (ii) Vitamin A, 6,000 units, and vitamin D, 1,000 units were given in the form of one capsule (adexolin) daily after a meal. A course lasted throughout the winter. (iii) A mixed vaccine of organisms found in the upper respiratory passages was employed. Four injections were given subcutaneously at 5-day intervals, starting with 0.5 c.cm. and increasing to 1 c.cm. for the 3 subsequent doses. (iv) Mixed vaccines in a dried form in capsules for oral administration. They were given on an empty stomach one a day for the first week and then one a week throughout the winter. In numbers of patients treated by (iii) and (iv) there seemed to be an increased susceptibility to colds. A large control group was established, the members of which did not receive any prophylactic treatment but were free to treat colds by ordinary methods. It was found that the only method of real value was ultra-violet irradiation, which reduced both the severity and the number of colds. A large percentage of patients treated by dissolved vaccines obtained complete relief from colds, although they had suffered during previous winters. The results, however, were not striking.

'Cold Vaccines'

In an attempt to estimate the prophylactic value of 'cold vaccines', I. J. Hauser and M. J. Hauser experimented (in Detroit) using a vaccine containing Friedländer's bacillus, 100,000,000 per c.cm.; *B. influenzae*, 200,000,000, pneumococcus, 100,000,000; streptococcus, 100,000,000, *Micrococcus catarrhalis*, 200,000,000, and staphylococcus, 400,000,000. To the first group it was given subcutaneously in a dosage of 0.25 c.cm. the first week, 0.5 c.cm. the second, 0.75 c.cm. the third week, and 1 c.cm. the fourth week. When practical, 1 c.cm. was given 1 month later. To the second group it was given intradermally, 0.05 c.cm. the first week, 0.1 c.cm. the second, 0.2 c.cm. the third, and 0.2 c.cm. the fourth week. Again 0.2 c.cm. was given a month later if the patient returned. A third control group was given injections at similar intervals of 0.5 c.cm. of sterile water each time. There were 200 persons in the first group and 100 in each of the 2 others. The injections were given from the third week in October to the middle of December, and, during the last 2 weeks in May, persons who had completed the series were interviewed. Data were obtained from 188 persons in the first group, 95 in the second, and 86 in the third. In the first group 74 per cent had had fewer colds than in the previous year, 6 per cent no colds, 18 per cent the same number as in the previous year, and 2 per cent more colds. In the second group 52.6 per cent had fewer colds, 11.6 per cent no colds, 32.6 per cent the same number as before, and 3.2 per cent more colds. In the third group, 60.5 per cent had fewer colds, 5.8 per cent no colds, 31.4 per cent the same number as before, and 2.3 per cent no colds. In the first group 79 per cent, in the second 61 per cent, and in the third 64 per cent felt that they had had one or more colds which rapidly aborted. The greatest improvement was obtained in those who had moderate or severe colds and who were treated subcutaneously with the vaccine, the percentage of improvement rising to 80. Nearly all the subjects expressed the desire to have vaccine immunization the following year.

H. S. Diehl, A. B. Baker, and D. W. Cowan compared 3 different vaccines recommended for the prevention of colds in catarrhal subjects. One vaccine was administered subcutaneously and contained pneumococci, streptococci, *B. influenzae*, *M. catarrhalis*, and staphylococci; another for oral administration contained these organisms except staphylococci, and the third, also given orally, was a streptococcal vaccine. To an elaborate control group was administered either sterile physiological sodium chloride subcutaneously, or lactose-filled capsules as a control for the vaccines administered orally. The group receiving vaccine subcutaneously showed an average of 25 per cent fewer colds per person than did the control group. This

reduction was hardly sufficient to justify the trouble involved in the intensive vaccination procedure. The control subjects, who believed they were receiving vaccine, also showed a reduction in the number of colds. The group to whom vaccine was administered orally showed as many colds as the control group.

Dangers of Nasal Sprays

Many nasal sprays used in the treatment of common cold are generally obtained not from physicians, but through advertisement, and T. E. Walsh and P. R. Cannon have shown that they may harm both the nasal mucosa and the lungs. These authors investigated the action of the substances from two angles, namely the vehicle in which the drugs are dissolved and the drugs themselves. The two commonest vehicles are mineral oil and water. The former may cause hyperactivity of the mucosa, and may retard the action of the cilia; the latter may also interfere with ciliary action and should be replaced by isotonic saline solution which does not. Oils may also be aspirated into the lung and cause lipid pneumonia. The authors report 3 cases of this condition. The drugs usually present in these preparations are antiseptics, astringents, and vasoconstrictors. Weak solutions of antiseptics were found to do no harm, but their antiseptic action was doubtful. Astringents cause anosmia, and in some cases cessation of ciliary action. Weak saline solution of ephedrine was the only vasoconstrictor found to have no harmful effect on the ciliary action and flow of mucus.

Walsh and Cannon then studied the early changes in the lungs of normal rabbits after the intranasal instillation of medicated oily and watery solutions of antiseptics, astringents, and vasoconstrictors. They found that oily solutions, applied to the nose, quickly passed to the lungs where they caused oedema and, ultimately, lipid pneumonia. They also carried bacteria from the nose into the lungs and granulomatous pulmonary lesions containing oil could be demonstrated in some cases. Watery solutions also entered the lungs causing oedema, focal necrosis, purulent bronchitis, and broncho-pneumonia. Isotonic saline solutions of vasoconstrictors, such as ephedrine, caused no damage and the authors considered that this was the only safe solution to use for intranasal medication.

Diehl, H. S., Baker, A. B., and Cowan, D. W. (1938) *J. Amer. med. Ass.*, **111**, 1168.

Hauser, I. J., and Hauser, M. J. (1939) *Arch. Otolaryng., Chicago*, **29**, 704.

Sherman, J. B. (1938) *Brit. med. J.*, **2**, 903

Walsh, T. E., and Cannon, P. R. (1938) *Ann. Otol., etc., St. Louis*, **47**, 579.

COLIFORM BACILLUS INFECTIONS

See also Vol. III, p. 281, and Cumulative Supplement, Key No. 249.

Treatment

H. Droller, insisting on the urgent necessity of treatment for all urinary infections, however slight, until the urine becomes alkaline, compares and contrasts the therapeutic values of mandelic acid and sulphanilamide. (i) Mandelic acid was administered as calcium mandelate (mandecal). Its greatest success is against *Bact. coli* and enterococci, but it usually fails in *B. proteus* and staphylococcal infections. The renal function should be good, so that the urine may speedily attain a pH of 5.5 or less. Of 31 cases treated with mandelic acid, 22 were cured (71 per cent). (ii) Sulphanilamide acts better in an alkaline medium and is directly bactericidal. Its greatest success was with mixed infections and in the presence of haemolytic streptococci and *B. proteus*. It was employed in 20 cases, and achieved complete success in 15 of them (75 per cent). The sulphanilamide treatment is much cheaper than its rival.

Sulphanilamide

C. J. Gessler and A. Lippens found that only little work had been done on the treatment of *Bact. coli* infections of the urinary tract with sulphanilamide. Of their 38 cases 19 were acute and 19 chronic. In the acute cases sulphanilamide relieved the fever and disturbances of micturition in 2 days. They recommend 3 g. daily for the first 2 days, and then 2 g. daily for 5 or 8 days. They had only one recurrence in 6 months. In their chronic cases—which had lasted for years—one

patient was resistant to the treatment and one had a recurrence after 6 months. The rest have been cured completely. The dosage of sulphanilamide was 3 g. daily for 2 days, 2 g. daily until the urine is clear, and then 1.5 g. for a few days.

Monoethanolamine Mandelate

E. Rupel and R. C. Travis, in an attempt to administer mandelic acid in a form acceptable to the patient and non-irritating to the stomach, treated some 24 patients with a specially developed enteric-coated tablet, timed for disintegration. Coated tablets of barium sulphate had been given previously. The mandelic acid salt selected was monoethanolamine mandelate (0.325 g.) to which was added 0.227 g. of ammonium chloride in each tablet. X-ray plates demonstrated the actual time of disintegration, which was complete in from 6 to 8 hours. These tablets promise a field of application when mandelic acid is indicated but ordinary preparations cannot be tolerated.

Droller, H. (1938) *Brit. med. J.*, **2**, 657.

Gessler, C. J., and Lippens, A. (1939) *Pr. méd.*, **7**, 124.

Rupel, E., and Travis, R. C. (1939) *J. Urol.*, **41**, 622.

COLITIS

See also Vol III, p. 292.

Ulcerative Colitis

Aetiology

An attempt was made by E. Wittkower (1938, a) to discover the aetiology of ulcerative colitis. A group of 41 cases was divided into 4 classes, based on childhood characteristics, which were found in most cases to have become accentuated in the adults. Long-standing psychological abnormalities were found in 38 of the 41 patients, and mental disturbances frequently preceded the onset, increase, or return of symptoms. The only constant causal factor was considered to be the occurrence of the disease in psychologically abnormal individuals under emotional stress.

Pathogenesis

P. W. Brown and J. A. Bagen attempt to draw a relationship between bacillary dysentery and subsequent chronic ulcerative colitis, but intensive cultural and serological investigations of the lesions of typical chronic thrombo-ulcerative colitis for organisms of the *Shigella* variety have yielded, for the most part, negative results. A follow-up study of 122 cases, investigated by Felsen in 1934, showed that regional enteritis or chronic ulcerative colitis developed later in 10 per cent. Kinsella reported on 140 cases of epidemic dysentery occurring in 1921, and found that, in 45, cultures of the stools yielded *Shigella paradysenteriae*. Review of all cases 16 years later showed the development of chronic ulcerative colitis in only one case. Further, the incidence of chronic intestinal ulceration, following wide-spread dysentery epidemics during wars, is exceedingly small. The authors conclude that they do not feel that there is sufficient evidence to suggest that the *Shigella* group of organisms is the cause of chronic thrombo-ulcerative colitis.

Treatment

Neoprontosil.—Neoprontosil (prontosil soluble) was recommended by A. F. Brown, W. E. Herrell, and J. A. Bagen, in ulcerative colitis; 4 to 5.32 g. of the drug were divided into 5 equal doses which were given at equal intervals throughout 24 hours, for a period of 10 to 14 days. Then for 10 to 14 days either no drug or 2.64 g. was given daily, and at the end of this period another course of full doses of the drug was prescribed. In many cases this treatment was followed by freedom for many months from toxic manifestations.

Liver extract.—G. Cheney (1939, a) treated 8 cases of idiopathic ulcerative colitis with highly concentrated liver extract. In 7 cases the treatment caused remissions of the disease and the eighth case was not sufficiently studied to assess the result of the treatment. The dose of the extract varies for individual cases, but Cheney considered that every patient should receive as a trial intramuscular injections of 10 units, 3 times a week, for the first month; 20 units a week for the second month, and a maintenance dose of 20 units every other week afterwards. It may be necessary to increase or decrease the maintenance dose in some cases. Reticulogen was the drug used in this series. The improvement in the condition was manifested clinically

by a diminution of the diarrhoea, an increase in weight, and a reduction in the amount of blood and pus, especially pus, in the stools. Proctoscopic examination in 6 of the cases showed healing of the mucous membrane. The mode of action of liver extract in ulcerative colitis is unknown but the factor responsible is not vitamins B₁ or B₂, or the G fraction of Cohn.

Vitamin B₁ and liver.—Vitamin B₁ was used alone and in conjunction with liver therapy by G. Cheney (1939, b) in cases of ulcerative colitis, mucous colitis, and chronic diarrhoea of unknown origin. Some cases responded to oral treatment, while others were only improved when hypodermic injections were given. Cases of ulcerative colitis were treated with liver extract administered parenterally with vitamin B₁ therapy, and improvement occurred in 10 out of 11 cases during the first month. Healing of the ulcers was observed, and after remissions a maintenance dose of 1 c.cm. of parenteral liver extract with vitamin B₁ every one to 3 weeks appeared to prevent recurrence. It was considered that the value of liver extract in these cases lay mainly in some as yet unidentified substance contained therein, and not in the vitamin B₁ or B₂ content. It was found in all 3 types that relapses were frequent when treatment was stopped.

Cod-liver oil enemas.—H. Gainsborough reported 6 cases of ulcerative colitis treated with cod-liver oil retention enemas. The diarrhoea and bowel irritability were first reduced by rest, a high-calorie diet, starch and opium enemas, and if necessary morphine, so that the patient was capable of retaining the oil enema. Two fluid ounces of oil were first used, and this rose to 8 fl. oz. by increases of 2 fl. oz., if the patient proved capable of retaining that amount. At first the injection was given during the day but, when the patient became able to retain it for some time, it was given in the evening and retained throughout the night. If X-ray examination showed the upper or transverse colon to be involved, the bed was tilted upwards for about 1 hour after the injection. Three of the patients were cured, and have been observed for 2 years without relapses. Two more obtained benefit but relapsed, one of these receiving benefit from further treatment. The sixth patient showed some improvement but, as haemorrhage persisted, an ileostomy was performed after which he died. The cases which responded best were those with the shortest previous history.

Combined Cod-liver Oil and Drug Therapy

R. R. Best treated 17 cases of ulcerative colitis with a course each of yatren, acriflavine, gentian violet, and cod-liver oil. The 3 first were given orally and by rectal instillation for 5 days each. Yatren was given first, in the form of one tablet by mouth 3 times a day and at bedtime, with a daily rectal instillation of 8 fluid ounces of a 1 per cent solution of yatren, following a saline enema. Acriflavine was then administered as a $\frac{1}{2}$ -grain tablet 3 times a day and at bedtime with instillation of 8 fluid ounces of a 1 in 5,000 solution. Gentian violet was then given in the same manner as the acriflavine. Daily rectal instillations of 4 fluid ounces of cod-liver oil followed. Immediately afterwards the ulcerated mucosa improved in appearance, the necrotic greyish areas becoming bright red with definite evidence of active epithelialization, and rapid symptomatic response occurred in most cases. Of the cases treated, 76 per cent have shown virtually no symptoms for periods varying from 3 to 22 months. Several showed some degree of incomplete healing, but only 2 showed marked residual ulceration. It was not found that improvement resulted from the use of cod-liver oil alone, but only when used after a course each of yatren, acriflavine, and gentian violet.

Larocain.—L. Bayer reported the use of local anaesthesia in the treatment of gastro-intestinal conditions. The author's first observations were based on the effect of larocain lavage of the stomach in cases of peptic ulcer; he was able to prove, with adequate X-ray controls, that this treatment not only stopped pain most effectively, but that it also greatly improved the condition of the patient. A great percentage of cases which showed definite signs of ulcer in the X-ray prior to larocain lavage were found to be normal after conclusion of the treatment. Further observations, made over a period of 5 years, showed the astounding effect on ulcerative colitis. In colitis 1,000 c.cm. of larocain were administered through a cecostomy; the patients so treated all improved immediately and were able to leave hospital 4 to 6 weeks later without further medication. The author warned against the indiscriminate use of this therapy, as it must not be used in cases of possible perforation.

Psychotherapy.—E. Wittkower (1939, b) discussed the indications for psychotherapy

in early cases of ulcerative colitis. In a series of 40 unselected cases, 37 were antedated by psychological abnormalities, neuroses, or psychoses. He could not establish any uniform type of person but obsessionals and hysterics were prominent.

Vaccine therapy.—During 11 years M. H. Streicher observed 570 cases of chronic ulcerative colitis, 217 being seen at weekly or fortnightly intervals for periods varying from one to 8 years with regular proctoscopic and stool examinations. The patients were put on a standard diet and multivalent vaccine was injected at weekly intervals. It was difficult to assess the exact point of healing in this condition and, although curtailment of diarrhoea, diminution in the amount of blood and pus in the faeces, and the alleviation of abdominal pain helped in determining the progress of the patient, the real criterion was the appearance of the mucosa on proctoscopic examination. Patients tended to relapse in the presence of infection elsewhere, such as acute respiratory disease. In this series 80 per cent of patients were either cured or improved, less than 3 per cent died, and the remaining 17 per cent were either not improved or suffered a complication which terminated fatally. The commonest complications were polyposis, stenosis, perforation, malignant disease, and perirectal abscess. The management of choice in chronic ulcerative colitis was rest in bed, dietary regime, vaccines, blood transfusions, and the removal of focal sepsis. Streicher considered that surgical interference should be reserved for acute complications.

Surgery.—T. E. Jones enumerates the complications of ulcerative colitis which furnish definite indications for surgery, namely the presence of stricture, polyposis or neoplasm, perirectal abscess, and regional or right-sided ulcerative colitis. In 93 per cent of cases examined by him, the disease started in the rectum and extended upwards in the colon. The use of sulphanilamide in 11 cases produced an unusually favourable initial response in 8. In the acute fulminating form acute or subacute perforations may occur, and laparotomy for closure of the perforation and drainage of the peritoneal cavity were practically worthless. Medical management should be employed in this type for 3 or 4 weeks and, if improvement has not followed, ileostomy should be considered. In the moderately severe cases, surgical measures were adopted and it is possible that colostomy can be performed instead of waiting until an ileostomy is required. Appendicostomy and caecostomy for irrigation, if not curative, produced some improvement and made the patient more comfortable. Colostomy, if performed, should be at a considerable distance proximal to the affected part of the colon and, if the sigmoid is at all involved, in the transverse colon. The value of a loop colostomy is contested and the bowel and its mesentery are divided for some distance so as to obviate the jumping over of the infection. Irrigation of the distal loop is of considerable value. In 137 cases of chronic ulcerative colitis examined radiographically at the Cleveland Clinic in 10 years fully one half were limited to the rectum or left half of the colon.

Bayer, L. (1939) *Med. Klinik*, **35**, 675.

Best, R. R. (1938) *Amer. J. digest. Dis.*, **5**, 426.

Brown, A. E., Herrell, W. E., and Bargen, J. A. (1938) *Proc. Mayo Clin.*, **13**, 561.

Brown, P. W. and Bargen, J. A. (1938) *Amer. J. digest. Dis.*, **5**, 562.

Cheney, G. (1939, a) *Arch. intern. Med.*, **63**, 813.

— (1939, b) *Amer. J. digest. Dis.*, **6**, 161.

Gainsborough, H. (1939) *Lancet*, **1**, 1319.

Jones, T. E. (1938) *J. Amer. med. Ass.*, **111**, 2076.

Streicher, M. H. (1938) *Amer. J. digest. Dis.*, **5**, 361.*

Wittkower, E. (1938, a) *J. ment. Sci.*, **84**, 1064.

— (1938, b) *Brit. med. J.*, **2**, 1356.

COLON, CARCINOMA OF

See also Vol. III, p. 317.

Aetiology

Adenocarcinoma of the large intestine is reported by M. T. Macklin and C. C. Macklin in cases of presumably dizygotic twin brothers. In case 1, aged 58, X-ray examination showed an obstructive lesion at the proximal end of the sigmoid colon.

A resection was performed and the patient died 7 weeks later. After a further 18 months, case 2, then aged 60, was found to have a new growth in the lower part of the ampulla of the rectum. An abdomino-perineal resection of the rectum was performed, and 10 days later a second operation to relieve obstruction of the small intestine was carried out. The patient died the same day. The immediate family history revealed no evidence of malignant disease, and a survey of the literature failed to reveal another case in which both twins suffered from carcinoma of the large intestine.

Macklin, M. T., and Macklin, C. C. (1939) *Arch. Path.*, **27**, 133.

CONCUSSION AND COMPRESSION

See also Vol. III, p. 355, and Cumulative Supplement, Key No. 255.

Diagnosis

W. C. Stevenson emphasized the importance of taking the temperature every 15 to 30 minutes in cases of head injury, diagnosis of the extent of the damage resting mainly on the level to which the temperature rises. In concussion or contusion-laceration the highest point is usually 100.5° F., from which it declines. In cases of acute cerebral haemorrhage a temperature of 104° F. may be attained. When the systolic blood pressure is increased over 175 and the pulse rate falls, lumbar puncture should be carried out and, in adults, 15 c.cm. of cerebrospinal fluid removed.

Stevenson, W. C. (1938) *Canad. med. Ass. J.*, **39**, 338.

CONJUNCTIVA, INJURIES AND DISEASES

See also Vol. III, p. 365; Cumulative Supplement, Key No. 256, and p. 128 of this volume.

Lime Burns

Treatment

Ammonium chloride as solvent.—G. C. Pether considered the treatment of lime in the eye and investigated the ability of solvent neutral solutions. The immediate removal of all large particles could be carried out by the medical attendant, if he is available, by a spud, a fine needle, or other suitable instrument, or in his absence by ambulance men at the works by a camel-hair brush, smeared with a mixture of equal parts of liquid and soft paraffin, followed by prolonged irrigation with a solvent. From a series of experiments, Pether found that a 4 per cent solution of ammonium chloride was the best solvent available. It was accordingly employed clinically and with encouraging results. When tried on his own eye Pether found that it caused less smarting than the boric acid solution usually employed. Its use need not be limited to the first irrigation or even to the first 24 hours. It may be employed beyond this time. If kept for a long time, the ammonium chloride solution may grow a mould; this may be prevented by the addition of a small quantity of preservative. It was possible that the irritation of the ammonium chloride irrigating solution might be advantageously diminished by the addition of an analgesic, but this remained to be tried. Removal of lime particles from the eye by an instrument was usually impossible until the eye had been anaesthetized, and Moss had found that 0.5 per cent decicain, which was neutral, was less painful than cocaine hydrochloride or butyn which were acid.

Moss (1936) *Med. surg. J.*, **89**, 302.

Pether, G. C. (1939) *Brit. med. J.*, **1**, 668.

Phlyctenular Conjunctivitis

Aetiology

L. B. Burgin and H. L. Higgins stated that with the fall in the incidence of phlyctenular conjunctivitis in the United States since the War 1914–18 there had been a decrease in all forms of tuberculosis, though pulmonary tuberculosis had not decreased as much as surgical. Hospital statistics for 1935 and 1936 in Boston showed

that its incidence was only 7.5 per cent of that 25 years ago. They examined 502 children with phlyctens and found that 300 gave positive reactions to tuberculin tests, and 109 showed clinical or radiological evidence of tuberculosis. Girls seemed to be more liable than boys to phlyctenulosis. The nutritional condition of the children as a group was normal. Although phlyctens were considered to be tuberculous in origin they contained neither tubercle bacilli nor giant cells. In 1927 Casparis stated that phlyctens were due to local sensitization of the conjunctival epithelium and/or the cornea to the tubercle bacillus. That phlyctens had decreased not with pulmonary tuberculosis, but with surgical, which is usually bovine, supported this view. Since the War 1914-18 increasing quantities of milk had been pasteurized and therefore fewer children had become sensitized to the tubercle bacillus. Further, the infecting tubercle bacillus in dust had become less prevalent with the introduction of hard roads and strict hygienic measures. There was evidence that the phlyctenule was an allergic manifestation in the patients with a positive tuberculin test. According to the authors the condition should probably be divided into 2 types, tuberculous and non-tuberculous, the cause of the non-tuberculous being unknown.

Burgin, L. B., and Higgins, H. L. (1938) *Amer. J. Dis. Child.*, **56**, 239.

Acute Papillary Conjunctivitis

Clinical Picture

P. Thygeson presented a report of an epidemic of acute papillary conjunctivitis, which is identified with Beal's conjunctivitis.

The principal characteristics of the disease were (i) follicular hypertrophy of the conjunctiva most marked in the lower fornix, (ii) an enlarged pre-auricular gland; (iii) scanty secretion consisting predominantly of mononuclear cells. Complete resolution takes place in from 1 to 3 weeks. Although closely resembling the follicular type of inclusion conjunctivitis, this type demonstrated no inclusion bodies, but a predominance of mononuclear cells. This condition had previously been designated as an acute catarrhal conjunctivitis of unknown aetiology, but possibly due to a virus.

Thygeson, P. (1938) *Amer. J. Ophthalm.*, **21**, 1017.

Hypopyon

In Mine-Workers

A. J. Rhodes noticed that more than half the cases of hypopyon ulcer attending the Eye Department of the Royal Infirmary of Edinburgh occurred in mine-workers working with coal or shale. Some of these ulcers were traumatic in origin, but the majority were infective. He therefore investigated the bacteria present in the conjunctival sacs of the workers. He examined 658 healthy coal mine-workers and found potentially pathogenic organisms. They were *Strep. viridans*, pneumococcus, diplobacillus of Morax, haemophilic bacilli, and *Bact. coli*. The workers were exposed to corneal trauma; the miners and brushers were more liable to hypopyon ulcer. In 189 shale workers he found the same conjunctival flora. He therefore concluded that it was the bacterial content of the mine-worker's conjunctival sac which made him peculiarly liable to hypopyon ulcer.

Rhodes, A. J. (1939) *Brit. J. Ophthalm.*, **23**, 25.

Staphylococcal Conjunctivitis

Treatment

Staphylococcus toxoid. -P. Thygeson treated 57 patients suffering from conjunctivitis, presumably due to toxigenic staphylococci, by immunization with staphylococcus toxoid. All had resisted local treatment for at least 2 months. The toxoid was given twice a week, the initial injection being 0.01 c.cm. of dilution No. 2. The dose was increased to a maximum of 1 c.cm. by stages of 0.02, 0.04, 0.06, 0.08, 0.1, 0.2, 0.6, and 0.8 c.cm. Twenty-one of the patients showed healing, 19 showed clinical improvement, and 17 no improvement. Cultures from 24 of the patients became negative after the treatment. Eight in whom healing occurred relapsed but recovered after a second course of toxoid therapy. This relapse appeared to be related to the failure of the treatment to eliminate the causal organism.

Thygeson, P. (1938) *Arch. Ophthalm.*, N.Y., **20**, 271.

Gonococcal Ophthalmia**Treatment**

Sulphanilamide.—The use of sulphanilamide in 8 cases of gonococcal ophthalmia is discussed by L. J. and R. F. Fernandez. A daily dosage of 2.6 g. was given for the first 3 days, and thereafter 1.95 g. each day. Two cases commenced with 3.9 g. for 3 days, 2.6 g. for 3 days, and finally 1.95 g. daily. Excellent results were obtained in a period varying from 9 to 21 days, and it was considered that the drug exercised a bacteriostatic action on the organisms, holding them in check until the natural defence mechanism of the body was mobilized. For this reason too early discontinuance of the drug was considered inadvisable.

S. H. McKee reported a case of unilateral gonococcal ophthalmia in a man of 23 years which was successfully treated with sulphanilamide. On admission the discharge from the eye showed innumerable gonococci. The eye was irrigated frequently with boric acid solution followed by the instillation of a few drops of 25 per cent solution of mild silver protein. The other eye was protected with a Bullar's shield. The patient was also given 15 grains of sulphanilamide with 5 grains of sodium bicarbonate every 6 hours. By the third day the amount of the discharge was reduced, and on the fifth day it had almost disappeared, and no gonococci were found in it. On the seventh day the patient was discharged from hospital feeling perfectly well. This is a great improvement on the treatment of the disease without the use of sulphanilamide, when the condition often takes 5 or 6 weeks to cure, and gonococci may persist in the discharge for as long as 35 days.

Fernandez, L. J., and Fernandez, R. F. (1938) *Amer. J. Ophthalm.*, **21**, 763.

McKee, S. H. (1939) *Arch. Ophthalm.*, N.Y., **21**, 1035.

Ophthalmia Neonatorum**Treatment**

Sulphanilamide.—The use of sulphanilamide in the treatment of ophthalmia neonatorum was reviewed by M. W. Michels, who found that, in a group of 15 children with ages ranging from 5 days to 3 years, the period of stay in hospital was reduced to 5.8 days as compared with 28.5 in the control group. There was a rapid decrease in the swelling and discharge, and in patients with red, chemotic, bulbar conjunctivae who had swollen retrotarsal folds and lids, these manifestations cleared up quickly. Dosage was estimated on the basis of 1 grain per 1 lb. body weight daily with equal amounts of sodium bicarbonate. No complications were noted. Two of the patients showed corneal involvement which did not proceed to perforation; 6 showed bilateral involvement.

Michels, M. W. (1938) *J. Pediatr.*, **13**, 527.

CONVULSIONS IN INFANCY AND CHILDHOOD

See also Vol. III, p. 406.

Treatment**Brilliant Vital Red**

S. Cobb *et al.* gave brilliant vital red intravenously to 10 children with various types of convulsions. The dye was injected until the patient became red, with in some cases red urine accompanied by albuminuria and red stools; the dosage varied from 115 to 1,396 c.cm. The colour disappeared from the skin in 2 to 3 months. Seven of the patients showed a temporary reduction in the number of convulsions while the vital red was being administered; 6 showed a sustained improvement, but in 3 of these phenobarbitone was also used; one patient had complete remission of the convulsions. Two patients treated with neoprontosil (prontosil soluble) showed marked diminution in the convulsions, and no harmful effects.

Dihydrotachysterol in Post-Operative Tetany

L. M. Hurxthal and T. S. Claiborne treated 6 cases of post-operative tetany of 2 or more years' duration with dihydrotachysterol (A.T. 10), a derivative of irradiated ergosterol. All calcium by mouth was stopped for a period ranging from

2 to 4 weeks and A.T. 10 was given in amounts of 12 to 20 c.cm. for the first 4 or 5 days in mild cases. This was then reduced to 1 c.cm. daily, or every other day. Larger initial doses were given in more severe cases and the routine dose ranged from 1 to 3 c.cm. daily. Later, calcium was given orally. Except when the blood calcium rose above normal, no toxic symptoms were observed. Calcium given by mouth reduced the amount of A.T. 10 which was necessary. The daily requirements of this substance appeared to be 2 to 5 c.cm. in mild cases, while the more severe required larger doses. It was found advisable to determine the correct dosage in individual cases by frequent determination of the blood-calcium level. One patient underwent successful pregnancy and delivery with combined A.T. 10 and calcium therapy. The high cost of this preparation made its use undesirable in mild cases which could be controlled by oral calcium lactate.

Complication of Calcium Therapy

W. R. Shannon reported 2 cases in which calcium salts, given for severe tetany in the new-born, were precipitated not only at the site of injection of calcium gluconate but also at distant parts in the body. In one case X-ray examination showed the presence of calcium salts in the walls of the arteries above and below both knee-joints, and in the other deposits were seen in the right lung. Resorption occurred without any permanent damage. It was suggested that this may also occur after the intravenous and oral administration of calcium salts, and that in patients with a low blood-calcium parathyroid extract may be a safer treatment.

Cobb, S., Cohen, M. E., and Ney, J. (1938) *Arch. Neurol. Psychiat., Chicago*, **40**, 1156.

Hurxthal, L. M., and Claiborne, T. S. (1939) *New Engl. J. Med.*, **220**, 911.

Shannon, W. R. (1938) *Amer. J. Dis. Child.*, **56**, 1046.

CORNEA, INJURIES AND DISEASES

See also Vol. III, p. 424; Cumulative Supplement, Key No. 260; and p. 128 of this volume.

Ulcers

Treatment

Methyl salicylate.—S. H. McKee treated satisfactorily over 20 cases of serpiginous ulcer of the cornea with methyl salicylate by a modification of Sabatzky's method. After anaesthetization with a 1 per cent solution of phenacaine hydrochloride, the ulcerated area was dried, and the oil rubbed in with a round-ended wooden applicator, the surrounding area being kept dry. After 2 or 3 minutes, the eye was bandaged and the patient was put to bed. Rest and tonics were given, and the treatment was repeated 3 or 4 times. No other cauterization was used. The treatment obviated the dense scars of the actual cautery, and was not as intensely painful as had been reported. McKee describes 5 cases; 2 in which Gram-positive diplococci had been grown from the smear from the ulcer, and one suffering from an infected perforating wound of the cornea, in which the methyl salicylate treatment was used with very satisfactory results.

McKee, S. H. (1939) *Arch. Ophthalm., N.Y.*, **21**, 121.

Symptomatic Affections

Acute Epidemic Superficial Punctate Keratitis

L. C. Hobson reports on 16 cases of acute epidemic superficial punctate keratitis. In 15 the onset was accompanied by violent bilateral conjunctivitis, about equally severe in each eye in contrast with the subsequent corneal symptoms which affected one eye more than the other. Photophobia and lacrimation were very pronounced. The initial conjunctivitis lasted for 10 to 14 days. Repeated smears and cultures taken from the conjunctival cul-de-sacs of all patients failed to reveal the presence of organisms. Dimness of vision did not appear until the development of corneal symptoms which began with a haziness of the cornea. The lesions, which consisted of masses of cells held together by fibrin, chiefly involved the second layer of the

cornea, and appeared as minute opaque grayish dots, from 20 to 100, the majority showing a tendency to be aggregated in triangles, base downwards. None of the corneas would stain with fluorescein. The more severe cases were complicated by a low-grade iritis. The aetiology of this disease remains obscure, although most observers associate the condition with minor focal infections of the eyes, teeth, and throat. According to Hobson this particular epidemic had an allergic basis. Treatment for the most part is symptomatic: the patient is kept in a dark room and hot or cold compresses are applied locally for relief of pain. Eye drops do not do any good. When the pain is more severe the instillation of pontocaine solution or ointment is recommended. Cocaine is contra-indicated in view of the diseased corneal epithelium. In the later stages a 5 to 10 per cent solution or ointment of dionin is recommended. After the initial irritant symptoms have passed off, a marked anaesthetic effect is observed. Quinine bisulphate is one of the more recent remedies, but has not any anaesthetic effect. No treatment has yet been devised which will definitely hasten the absorption of the deposits, which have been known to remain for as long as 2 years or more, and in some cases permanent damage results.

Keratitis Ramificata Superficialis

A new ophthalmological disease was originally recognized in 1908 and an account of it published in 1914 by W. A. Wille of Java, but did not attract any attention; he has now written a paper on keratitis ramificata superficialis and its connexion with asthenopia, blepharospasmus nictitans, and pterygium. Keratitis ramificata superficialis was quite distinct from the well-known keratitis ramificata or dendritica. It was very common in the tropics and during the summer Wille had recognized it in England and Denmark. The reason why the disease had so long been unrecognized was stated to be that the living cornea was covered by lacrimal secretion and so the lesion was not obvious. The change was essentially epithelial and resulted in denudation of the cornea and the formation of a branched figure. In order to see the lesion the lacrimal fluid must be allowed to evaporate from the cornea, and therefore the eye must be kept open; this was facilitated by the instillation of cocaine or pantocain. The commonest symptoms were asthenopia, blepharospasm nictitans (the cure of which accompanied that of the keratitis), headache, epiphora, photophobia, and occasionally vertigo. Treatment involved protection of the eyes against glare, wind, and dust, and the use of dark spectacles out of doors. The eyes must be rested from reading and writing. The author recommends the use of a 2 per cent solution of soluble fluorescein preserved with mercuric chloride, 1 in 10,000; this solution is dropped into the eyes five times a day. It might be necessary to brush the cornea with 1 or 2 per cent solution of silver nitrate. It was also found that the instillation of antgonococcal serum 3 times a week for 1 to 1½ months effected a cure in obstinate cases. The author had found a high degree of keratitis in all cases of pterygium, and, because the head of the pterygium always withered when the keratitis was treated, he concluded that the pterygium was caused by the keratitis. He also discussed the connexion between keratitis and conjunctivitis aestivalis and concluded that they are two separate diseases of partly common aetiology.⁵

Hobson, L. C. (1938) *Amer. J. Ophthalm.*, **21**, 1153.

Wille, W. A. (1938) *Brit. J. Ophthalm.*, **22**, 705.

Degenerations

Arcus Senilis

Aetiology.—The arcus senilis common in old subjects is due to a deposit of lipoids in the periphery of the cornea, and also occurs in conditions associated with hypercholesterolaemia. N. L. Corkill described it in young subjects and reported it in 2 Sudanese army officers. Dietary deficiency, especially vitamin C, and bright sunlight produced this condition. It was also seen in Italian pellagrins and in Javanese natives. Arcus senilis might be a sign of chronic vitamin C subnutrition, which might be related to cholesterol metabolism.

Keratoconus

Vitamin D treatment.—From a study of 11 patients (18 eyes) suffering from various degrees of conicity, A. A. Knapp concluded that a supply of vitamin D had a definite place in the therapy of keratoconus. Seven had bilateral involvement, 3 had a right keratoconus, and one a left. Each of the 11 patients was given 60 drops of

viosterol (calciferol) after breakfast, and it was noticed that in every case there was considerable improvement. Calcium was also prescribed, the amount varying with the milk intake.

Corkill, N. L. (1938) *Ann. trop. Med. Parasit.*, **32**, 333.

Knapp, A. A. (1939) *Amer. J. Ophthalm.*, **22**, 289.

CORNS AND BUNIONS

See also Vol. III, p. 433.

Aetiology

E. Zurhelle stated that, on the basis of his experimental investigations, it can be assumed that callus, pigmentation, and hyperkeratosis in the epidermis are due to mechanical injuries which result in a colloidal alteration in parts of the tissue, characterized by a change from a sol to a gel. There is an accompanying dilatation of the vessels and a swelling of the epidermal cells, and the whole process can be demonstrated to be reversible. This reversion can be achieved if the limbs on which these transformations have occurred are rested and not used.

Zurhelle, E. (1939) *Derm. Wschr.*, **108**, 660.

CRANIAL NERVE AFFECTIONS

See also Vol. III, p. 470.

The Optic Nerve

Arachnoiditis Affecting the Optic Chiasma

Operative treatment.—A. Jirásek describes 7 cases in which operation was performed for arachnoiditis in the optic chiasma as a primary or secondary affection. One patient died; more or less marked improvement was observed in the other cases, but the final result could not be stated as the operation had been done only one or 2 years previously. Adhesions between the arachnoid and the chiasma as well as with the base of the brain were observed. Atrophy of the optic nerve was found in 5 cases. At operation compressed and adherent nerves as well as the chiasma were freed and a longitudinal incision was made in the sheath of the affected optic nerve.

Jirásek, A. (1939) *Wien. med. Wschr.*, **89**, 467.

The Seventh Nerve

Flattening of Nares as Diagnostic Aid

The nares are innervated by the seventh cranial nerve, and J. H. Leiner believed that they were more easily affected than the larger facial muscles in supra-nuclear, nuclear, or peripheral lesions of the nerve. Thus their relative position could be used as a means of early diagnosis. He found that, when the patient was unconscious, as in apoplexy, there was flattening of the nares on the side involved. In cases of hysterical and malingering hemiplegia there was no flattening. Fractures of the base of the skull, when the middle fossa was involved, led to total collapse of the nares on that side. He is now studying the use of the 'sniffing test' for the differential diagnosis between the reactions of supra- and infra-nuclear lesions, and as a guide to prognosis.

Leiner, J. H. (1938) *J. nerv. ment. Dis.*, **88**, 771.

CROHN'S DISEASE

See also Vol. III, p. 508; Cumulative Supplement, Key No. 277; and p. 49 of this volume.

Aetiology

Crohn's disease, regional ileitis, or regional enteritis has been investigated at the Mayo Clinic both bacteriologically and from the aspect of the morbid changes. R. E. Pumphrey from examination of 13 specimens concluded that the lesions may

be due to many different agents which induce a uniform change, but that what is the responsible agent is unknown. R. J. Coffey examined 21 cases in which the ileum was predominantly involved in a hyperplastic stenosing inflammatory process; in 10 cases the lesion had spread into the caecum, and in 6 cases there were external fistulae, all after operative interference, usually appendicectomy. There was evidence that, although the terminal portion of the ileum is chiefly and often solely involved, the intestine above or below may also be affected. Except when there is an active tuberculous lesion, for example of the lungs, there is no reason to regard the regional enteritis as tuberculous.

Coffey, R. J. (1938) *Proc. Mayo Clin.*, **13**, 541.

Pumphrey, R. E. (1938) *Proc. Mayo Clin.*, **13**, 539.

Clinical Picture

Infantilism as a Sequel

Infantilism due to Crohn's disease is reported by A. H. Logan and P. W. Brown. A girl, aged 16 years, who looked like one of 10 years of age, weighed 60 lb. and was 56½ inches tall. She had been ill for three years with abdominal pain and attacks of diarrhoea. There was a tender mass in the right lower part of the abdomen, and a barium sulphate enema of the colon showed the presence of a granuloma in the ileo-caecal region with a patchy distribution of ulcerative ileitis in the terminal part of the ileum. An ileo-colostomy was performed and in a year's time her weight had increased by 27 lb.

Logan, A. H., and Brown, P. W. (1938) *Proc. Mayo Clin.*, **13**, 335.

CYANOSIS, ENTEROGENOUS

See also Vol. III, p. 520; Cumulative Supplement, Key No. 279, and p. 176 of this volume.

Aetiology

Sulphanilamide

J. A. Bigler and M. Werner stated that cyanosis does not depend on the age of the patient, or on the size or duration of dosage with sulphanilamide. They have seen no harmful results from continuing treatment in the face of cyanosis. The main change is a darkening of the red blood-cells. When the blood serum separates it is found to have a normal colour, the change therefore occurring in the corpuscles and probably being due to some pigmentary change in the red blood-cells. The authors failed to confirm the finding of spectroscopic bands for sulphaemoglobin or methaemoglobin in the blood of cyanosed children. They failed to find a definite correlation between the cyanosis and the presence of non-functioning haemoglobin. Nor does the cyanosis depend on the oxygen saturation of the arterial blood. They are therefore unable to explain the phenomenon.

Bigler, J. A., and Werner, M. (1939) *Amer. J. Dis. Child.*, **57**, 1338.

Treatment

Methylene Blue

A. F. Hartmann *et al.* demonstrated that administration of sulphanilamide leads to methaemoglobin accumulation with consequent cyanosis and a reduction in the oxygen-carrying capacity of the blood, but that methylene blue rapidly reduces the methaemoglobin content. Spectacular reductions were shown when intravenous injections of methylene blue were given, the effect being practically complete in 30 minutes. It was shown that large doses of sulphanilamide may result in a deprivation of 37 per cent of the oxygen-carrying capacity of the blood, a serious consideration, particularly in cases of pulmonary disease. By the use of methylene blue, however, it is not necessary to curtail the administration of sulphanilamide; the 2 drugs can be given in combination with no apparent impairment of the therapeutic effects of the latter. In oral administration it is advisable to give methylene blue in divided doses over 24 hours at the same time as the sulphanilamide; when rapid results are required the intravenous route is used, but care must be taken to avoid perivenous infiltration, which may lead to necrosis. It has been

found that 0.1 to 0.2 c.cm. per kilogram of body weight of a 1 per cent aqueous solution of methylene blue converts all the methaemoglobin in the circulating erythrocytes into functionally-active haemoglobin within 45 minutes.

Methylene blue is considered to be only slightly toxic, though even moderate oral doses sometimes produce vomiting and diarrhoea.

Hartmann, A. F., Perley, A. M., and Barnett, H. L. (1938) *J. clin. Invest.*, **17**, 699.

DEAFNESS

See also Vol. III, p. 555; Cumulative Supplement, Key No. 284; and pp. 87 and 100 of this volume.

Diagnosis

Audiometric Examination

I. H. Jones and V. O. Knudsen explained the apparatus, principles, and standards of the audiometer, and enumerated its uses in routine practice. The audiometer can be used to measure the exact amount of hearing which a patient possesses both by air and bone conduction. If the hearing is impaired, how much that impairment is due to conductive or mechanical error and how much to perceptive or cochlear error can be ascertained. If audiometry fails to show which type of hearing aid is needed, careful speech articulation tests may elucidate the problem. The patient who has a loss of 25 decibels or more through the range of 256 to 4,096 cycles as shown by the audiometer, should have a hearing aid. If the impairment is conductive, a bone-conduction receiver is indicated; if primarily perceptive, an air-conduction type is necessary. If the loss is greater, and especially if it is mostly perceptive, a high quality vacuum-tube aid should be advised. This aid is also indicated when the loss is mostly perceptive, and at high rather than at low frequencies.

Jones, I. H., and Knudsen, V. O. (1938) *J. Amer. med. Ass.*, **111**, 597.

Middle-Ear Deafness

Treatment

Prostigmin.—Prostigmin was used by T. C. Davis and J. C. Rommel in 2 groups of cases, one consisting of 28 cases of acute obstruction of the Eustachian tube, the other of 29 cases of chronic deafness, both groups with tinnitus aurium. In the acute cases an average of 5 injections of prostigmin was effective in restoring hearing. Catheterization of the Eustachian tube was performed, and massage given. Dosage consisted of 1 c.cm. of a 1 in 2,000 solution every third to fifth day. Two patients had recurrences, but hearing returned to normal after further treatment. In the chronic group, reports are shown of 20 cases, in all except 2 of which improvement in hearing and relief of the tinnitus, either slight or marked, occurred. In the 2 cases mentioned reaction due to a thyroid condition prevented completion of treatment. The authors point out that this treatment, which is of real value in deafness and tinnitus, may be prolonged for chronic patients, but that injections may be administered indefinitely, in small doses and at suitable intervals, without toxic effects. Nasal obstructions and sinusitis should be treated first.

Davis, T. C., and Rommel, J. C. (1939) *Arch. Otolaryng.*, *Chicago*, **29**, 751.

Constitutional Deafness

Treatment

Oestrin.—The relationship between the two constitutional disabilities, atrophic rhinitis and progressive deafness, is discussed by H. Mortimer *et al.* From an examination of the cranial skiagrams of 70 cases of constitutional deafness, it was found that these patients suffered from a similar constitutional background to those with the nasal condition. The same defects also appeared in the same familial stock more often than has hitherto been realized. The specific relation between the sex glands and the nasal mucosa has been recognized, and after considerable study of groups of males and females suffering with the aural or nasal condition, or with

both, a series of 55 mixed cases of constitutional deafness was treated with daily nasal insufflation of 1 c.cm. of oil containing 1,000 international units of oestrin. Treatment lasted at least 3 months and in many cases up to 6, while some were treated intermittently for 2 years. Improvement in hearing followed treatment and the hearing of untreated patients appeared to deteriorate. It is not suggested that constitutional deafness is an endocrine disease.

Mortimer, H., Wright, R. P., Thomson, D. L., and Collip, J. B.
(1939) *Canad. med. Ass. J.*, **40**, 17.

Nerve Deafness

Actiology

E. Mellanby investigated the changes in the labyrinth capsules of young dogs fed for some months on a diet deficient in vitamin A and rich in cereals, and found degeneration varying in degree up to complete disappearance of the cochlear nerve, the cells of the spiral ganglion, and their central and peripheral branches. The vestibular division of the 8th nerve degenerated, but to a less degree. Overgrowth of bone in the modiolus and of the periosteal layer of the capsule near the brain occurred, and apparently caused the degenerative changes in the nerves by stretching, and pressing on, them. Serous labyrinthitis also developed in the cochlea, eventually producing degeneration of the sensory epithelium of the labyrinth, the organ of Corti, and the ampullae of the semicircular canals. The inclusion of potato instead of cereals in the diets reduced these abnormal changes. The base of the skull showed bony overgrowth, which may similarly explain the degeneration of cranial nerves, such as the optic and trigeminal.

Nearly one-third of deaf persons in the United States are children and, of 3,334 children examined, 62 per cent were found to be congenitally deaf. R. A. West investigated the action of quinine, given to the mother during pregnancy, on the auditory nerve of the foetus. A review of the literature shows that quinine bisulphate has a selective action on the 8th nerve and that quinine in massive doses administered to the pregnant woman tends to affect the foetus, with resulting hearing defects. Quinine sulphate given to an animal in massive doses produces degeneration of the myelin sheath of the auditory nerve. West did a controlled experiment on normal rabbits giving them a dose of quinine bisulphate by mouth equivalent to that given to the pregnant woman and found that the offspring at the age of 2 months showed degeneration in the auditory nerve, spiral ganglion, and peripheral neuron of the cochlear nerve.

Treatment

Nicotinic acid.—G. Selfridge pointed out that the significance of the various fractions of the B₃ complex has not yet been fully investigated nor the relation of these fractions to the degeneration of the peripheral nerves and general nervous system. Nicotinic acid and nicotinamide were used in 30 cases of chronic progressive deafness, their probable value being suggested in a series of experiments by Covell which showed a marked and rapid degeneration of the auditory nerve in vitamin B deficiencies. The quantity of nicotinic acid used was up to 60 mg., 3 times a day, continued for as long as 6 months. The results obtained showed a more rapid improvement in the air and bone-conduction audiometric curves than when vitamin B₃ or riboflavin was administered. In addition to acting as a vasodilator, nicotinic acid has a definite action in helping to remove calcium in the adhesions around the foot-plate of the stapes, in chronic progressive deafness.

Mellanby, E. (1938) *J. Physiol.*, **94**, 380.

Selfridge, G. (1939) *Ann. Otol. etc., St. Louis*, **48**, 39.

West, R. A. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 241.

Otosclerosis

Treatment

Vitamin and calcium therapy.—L. K. Guggenheim presents a comprehensive plan for the treatment of otosclerosis. The otosclerotic process consists of dystrophy of the bone, which is dependent upon a stage of preparedness of the capsule, called halisteresis, or loss of calcium. The enlargement of the otosclerotic process depends on the presence and extent of this halisteresis. It is suggested that close attention should be given to the diet which may be supplemented by 1,000 to 3,000 units of vitamin C

daily in the form of orange juice and 3,000 to 6,000 U.S.P. units of vitamin D daily in the form of fish oil. Dicalcium phosphate may be added and, in the presence of tinnitus, brewers' yeast or vitamin B complex.

Surgical.—J. Lempert described an operation for the improvement of hearing in otosclerosis. The object of the operation is to make a fenestra in the bony capsule of the external semicircular canal and to keep this fenestra permanently open. The operation must be carried out under strict aseptic technique and, if this is not maintained, there is danger of infection of the tympanic cavity, the mastoid antrum, and the labyrinth. Lempert operated on 23 patients and in 19 of them the hearing was improved. In the remainder bone conduction was very poor prior to operation, and was not improved after it. The fenestra in 22 of these patients remained open, but closed within 3 weeks in the twenty-third. Lempert believed that, if a fenestra is going to close, it does so almost immediately after operation, and, if it has not closed within 2 months, it will remain permanently open.

Guggenheimer, L. K. (1938) *Amer. J. Surg.*, **42**, 156.

Lempert, J. (1938) *Arch. Otolaryng.*, *Chicago*, **28**, 42.

DEATH, SUDDEN AND UNEXPECTED

See also Vol. III, p. 565.

Common Causes

J. R. Lisa and J. F. Hart recorded their anatomical observations on 70 patients in the New York City Hospital who died suddenly, namely, within 20 minutes of the onset of acute symptoms. As would be expected, the great majority were cardiac in origin. 49, or more than two-thirds, showed fatal changes in the heart. In 7 instances death was cerebral; in 4 due to pulmonary lesions; in 3 to spontaneous rupture of the aorta, such as occurs from syphilitic aortitis in the first, intra-pericardial, part of the aorta; in 3 to rupture of an aneurysm; in 2 to gastric accident; and in 1 only to status lymphaticus and to asphyxiation due to a bolus of food. The cardiac cases were subdivided into 8 groups: (i) Acute miliary infarction (12 cases); this condition, described by H. Roesler and L. A. Soloff (1935), consisted in small areas of necrosis. (ii) Acute toxic myocarditis (10 cases). (iii) Acute coronary thrombosis (9 cases); all the cases were in advanced life and showed extreme arteriosclerosis of the coronary vessels. (iv) Acute infective myocarditis (7 cases); in 5 instances there was also acute valvular endocarditis, and in 3 syphilitic myocardial change. (v) Acute rheumatic infection (4 cases); there were in these cases an enormous number and wide distribution of Aschoff's bodies. (vi) Acute interstitial involvement (3 cases). (vii) Heart block (2 cases). (viii) Aortic stenosis (1 case). Of the 4 cases of pulmonary origin 3 were due to pulmonary embolism. In 26 out of the 70 cases, or about one-third, the clinical diagnosis was confirmed by post-mortem examination.

Lisa, J. R., and Hart, J. F. (1939) *Arch. intern. Med.*, **64**, 43.

Roesler, H., and Soloff, L. A. (1935) *Ann. intern. Med.*, **9**, 477.

DENTAL SEPSIS IN RELATION TO SYSTEMIC DISEASE

See also Vol. III, p. 596, and Cumulative Supplement, Key No. 288.

Dental Sepsis in Adults -

In a survey of the conditions associated with immunity and susceptibility to dental caries Norman Bennett divided the factors involved into 3 as follows: (a) the structure of the teeth; the enamel was not a dead protecting covering for the dentine, it was influenced by the conditions of nutrition, and hypoplasia was caused by vitamin D deficiency (Mellanby); (b) the effect on the teeth, in health and disease, of substances brought by the blood under varying constitutional states; vitamin D deficiency, pregnancy, calcium lack, and acidosis had been incriminated; (c) the environment, namely, the saliva and its contents, bacteria such as *Bacillus acidophilus*, and chemicals such as sugar. Though a disease of civilization, dental caries was not confined to civilized races or times; a detailed consideration of the

incidence of caries throughout the world was given. Primitive foods protected against caries, whereas the food of civilized races and vitamin lack favoured its incidence. There had been too great a tendency to concentrate on a single factor, but all these 3 factors were operative, though in what proportion it was difficult to decide. It was, however, now possible to inhibit, if not to prevent, caries by a simple diet, based on consideration of vitamins rather than on calories; indeed among the better educated, as the result of sensible feeding of children from infancy, dental caries had become much less prevalent than it was 30 or 40 years ago. There was an antagonism between dental caries and parodontal disease.

Bennett, N. (1939) *Brit. dent. J.*, **66**, 103.

Mellanby, M. (1934) *Med. res. Coun., Lond., Spec. Rep. Ser.* No. 191, part 3.

DENTITION

See also Vol. III, p. 603.

Abnormal Dentition

G. F. Taylor and C. D. Marshall Day investigated 10 cases of severe clinical rickets in children from the Punjab to obtain data concerning the degree of dental decay present. The diet of these children was poor in protein and fat, meat and fresh fruit being almost entirely lacking and even the supply of milk and vegetables being very scanty. The diet comprised chiefly carbohydrates. Of the 10 cases, 4 were free from dental caries; the remaining 6 showed 14 cavities, the group average being 1.4 cavities. On the other hand, in a group of 800 middle-class Indian children, seen in Lahore, the dietary of whom was well balanced, an average of 6 cavities per child was noticed. From this evidence it appeared that diets short of vitamins A and D with accompanying calcium and phosphorus deficiency and rich in 'anticalcifying' cereals did not increase the liability to dental hypoplasia or dental caries.

Taylor, G. F., and Day, C. D. M. (1939) *Brit. med. J.*, **1**, 919.

DERMATITIS DUE TO INJURY AND POISONING INCLUDING FEIGNED ERUPTIONS

See also Vol. III, p. 609.

Toxic Dermatitis

Aetiology

Vaseline.—L. Hollander reported a case of sensitivity to vaseline in which a vesicular and vesiculo-papular eruption of the scalp and forehead accompanied by profuse irritation was associated with oedema of the upper and lower eyelids and cheeks. The patient was confined to hospital, and all possible causes eliminated by patch tests. A mask was applied and kept continually moist with a solution of aluminium acetate. The fact that the patient had used vaseline as a dressing for the hair was elicited, and vaseline was massaged into the arm 4 times daily. Two days later, an eruption appeared at the site of application, thus solving the problem of the aetiological agent. The author emphasized the necessity of applying the suspected irritant in the same manner as it would normally be used.

Citrus fruits.—H. Beerman *et al.* described the dermatoses which might arise from contact with citrus fruits. They divided the cutaneous manifestations into 4 groups: (i) true allergic reactions; (ii) reactions due to mycotic or parasitic contaminants; (iii) reactions due to dyes or preservative contaminants; and (iv) pseudo-allergic reactions. In considering the first, citrus fruits contain many substances which may give rise to allergy. The condition is usually limited to the hands, but the oil from the skins may get smeared on the face. Erythema, swelling, oedema, and vesiculation occur. Two cases of this type are reported, one occurring on the chin from drinking orange juice. In the mycotic and parasitic group, yeasts have been cultured from oranges which have produced a similar dermatitis in those not in contact with the fruit. Dermatitis may be produced by chemicals applied to hasten the ripening of the

fruit or to preserve its life. Among chemicals used thus are ethylene, paraffin, sodium borate, and hydrocyanic acid. In the pseudo-allergic group are placed patients who were sensitive to citrus fruits but whose dermatitis appeared to have another cause. Two such cases are reported in which avoidance of the fruits did not cure the dermatitis, although the patch tests were strongly positive. Twenty-seven normal subjects, patch tested with orange, lemon, and grape-fruit peels, were all negative to orange and grape-fruit peels, but 5 were positive to lemon peels. It was shown that the oil from lemon peel may be a cutaneous irritant in certain cases.

Beerman, H., Fondé, G. H., and Calloway, J. L. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 225.

Hollander, L. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 49.

DERMATITIS GANGRENOSA INFANTUM

M. L. Blatt *et al.* reported a case of dermatitis gangrenosa infantum occurring in a child aged 2 years and 11 months. The condition was characterized by fever, toxæmia, and papulo-ulcerative lesions, some scabbed with black eschar and some punched-out ulcers, over the entire body, especially the anterior chest and abdominal wall and the sacral region. The bases of the ulcers were necrotic and covered with pus. The oral mucosa was free from lesions and enlarged cervical glands were present. The heart and lungs were normal. The Wassermann and Kahn tests were negative. The patient was anaemic, but there was no leucocytosis and the differential count was normal. Photophobia due to phlyctenular keratitis was present. Haemolytic *Staphylococcus aureus* was cultured from the lesions, and from the blood stream.

The prognosis in this condition is grave, but the patient recovered after several weeks' treatment. The eye condition was healed by hot dressings, irrigations with boric acid, and instillation twice daily of atropine, 1 per cent. Wet dressings of a 25 per cent solution of urea were applied to the ulcerating lesions every 2 hours. When healing began the lesions were painted with a 1 per cent solution of methyl-rosaniline (methyl violet) until crusts formed. In the later stages adhesive strips were placed over the granulating areas. Many scars resulted. Because of the low level of ascorbic acid in the blood the diet was supplemented with ascorbic acid (100,000 units during 48 hours). Multiple small blood transfusions were given. The aetiology of the condition is not certain. It is thought by some to be tuberculous and by others to be a manifestation of vitamin deficiency.

Blatt, M. L., Stulik, C. K., and Nachman, A. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 407.

DERMATITIS HERPETIFORMIS

See also Vol. III, p. 627.

Aetiology

The biochemical manifestations in dermatitis herpetiformis, Dühring-Brocq's disease, were examined by R. Turpin *et al.* Certain characteristic changes were found, especially in the protein metabolism. There was a hypoproteinaemia which mainly affected the serum albumin, and led to lowering of the albumin-globulin ratio to 0.6 to 0.8; the globulin content of the serum remained unchanged. The liquid of the vesicles on the other hand had a very high level of protein, amounting to 33.1 to 45.8. Globulins were predominant, giving a ratio of 0.32 to 0.63. Lipoids remained unchanged, and cholesterol maintained its normal level. The lipid-albumin index remained normal. It was further found that ingestion of large amounts of sodium chloride increased the number of the vesicles, though the chlorine metabolism did not show abnormalities. Calcium metabolism, however, was disturbed; there was a marked diminution of protein-bound calcium. Ionized calcium, on the other hand, remained normal. Potassium was present in higher proportion than in normal subjects, which resulted in a potassium-calcium ratio of 4.1. Necropsy of a fatal case showed gross liver damage, hepatomegaly, and fatty degeneration. All these changes, coupled with the clinical symptoms, led the authors to believe that this disease is of an allergic nature.

Turpin, R., Chassagne, P., and Cavier, R. (1939) *Pr. méd.*, **47**, 933.

DIABETES INSIPIDUS

See also Vol. III, p. 639, and Cumulative Supplement, Key No. 295.

Aetiology

Carcinoma of the breast most often is the primary cause of a metastasis in the pituitary. L. Rimbaud and H. A. Huibert fully discussed a case of a primary mammary carcinoma with secondary growths in the lungs and the posterior pituitary, in which the onset of polyuria was the first indication of the pituitary metastasis.

Diabetes insipidus after diabetes mellitus.—In a paper on diabetes mellitus associated with lesions of the pituitary, E. McPherson reported the case of a man, aged 60, who after being on the verge of diabetic coma improved very greatly, but began to show severe intolerance to insulin and the symptoms of diabetes insipidus. It was suggested that in this patient the diabetes mellitus was due to hyperplasia of the eosinophil cells, as in acromegaly, and that the subsequent diabetes insipidus was due to the same lesion of the pituitary in a later stage of its development.

McPherson, E. (1939) *Glasg. med. J.*, **131**, 220.

Rimbaud, L., and Huibert, H. A. (1938) *Bull. Ass. franç. Cancer*, **31**, 555.

DIABETES MELLITUS

See also Vol. III, p. 644, and p. 67 of this volume.

Pathogenesis

E. M. Bridge and E. A. Winter sought to correlate the action of insulin in diabetes mellitus, with blood-sugar and the respiratory quotient, and with that purpose carried out various investigations and tests on 13 hospital patients, both children and adults, at different stages of treatment. Six determinations of both blood-sugar and respiratory quotient were made daily over a total of 30 days. No direct relation was observed between insulin action and respiratory quotient, and it was considered that, as borne out by animal experimentation, hypoglycaemia from over-dosage with insulin is not due to excessive carbohydrate combustion, but to an excessive deposit of glycogen in the muscles. It was suggested that the nature of the disturbance of carbohydrate metabolism in diabetics probably centred in the liver. The authors point out that removal of the liver from diabetic dogs resolves diabetic symptoms, and that there is a relation between the glycogen content of the liver, carbohydrate combustion, and respiratory quotient.

Bridge, E. M., and Winter, E. A. (1939) *Johns Hopk. Hosp. Bull.*, **64**, 257.

Clinical Picture*Co-existing Peptic Ulcer*

From a study of 3,525 cases of diabetes mellitus admitted to the Jewish Hospital of Brooklyn from 1913 to 1936, R. E. Rothenberg and I. Teicher found that only 9 patients had a co-existing peptic ulcer. Whereas the general incidence of peptic ulcer among hospital admissions during that period was 1.49 per cent, among diabetics it was only 0.25 per cent. This low incidence is thought to be explained by the fact that diabetic patients frequently show a lowered acid secretion, and there seems to be a definite relationship between gastric hyperacidity and ulcer formation. Ulcer symptomatology was atypical in most of these cases. The pain was not usually periodic, and little relief was afforded by alkalis or food. The diabetic condition was mild. The most successful therapeutic results were obtained by placing the patient on a Sippy diet, and regulating the diabetic symptoms with insulin injections. In diagnosing gastro-intestinal conditions in a known ulcer patient it is important to exclude the possibility of pancreatitis as the source of glycosuria. It is considered that operative procedures are undertaken with increased risk on patients in whom peptic ulcer co-exists with diabetes mellitus.

Rothenberg, R. E., and Teicher, I. (1938) *Amer. J. digest. Dis.*, **5**, 663.

Diagnosis

Relation between Urinary and Blood Sugar

A. Sindoni observed that the urinary sugar tests usually applied frequently give little indication of the true blood-sugar content. Comparisons were made between the blood-sugar and urinary sugar in patients treated with zinc-protamine-insulin and ordinary insulin, given separately, and in combination with each other, and a final group who received treatment by diet alone. Patients were made to void before breakfast; insulin was given after this, and all urine passed in the next 3 hours was examined for dextrose. One and 2 hours after breakfast specimens of venous blood were taken to estimate dextrose. In another group of patients, 24-hour specimens of urine were obtained and examined for dextrose, blood-sugar estimations being made one and 2 hours after breakfast. In the first group, which showed a total average blood-sugar level above normal, and in some cases over 200 mg. per 100 c.cm. no excretion of sugar was apparent in the urine. It was found that higher blood-sugar levels without glycosuria were present when both forms of insulin were combined, rather than when they were given separately, or when no insulin was given. A second group showed what might be considered an insignificant amount of sugar in the urine. These patients, who had high blood-sugar levels at the end of the first or second hour after breakfast, passed less dextrose than those who averaged low levels of blood-sugar.

In other cases, when ordinary insulin was given, the blood-sugar reached levels as high as 390 mg. per 100 c.cm. an hour after breakfast, but the 24-hour urine was normal. These high blood-sugar levels, with normal 24-hour urines, were also noted in the group which was given ordinary and protamine-zinc-insulin. Blood-sugar estimation must be carried out in every stage of the disease while the patient is under treatment, as the estimation of the urinary sugar gives unreliable findings. Hyperglycaemia, and not glycosuria, has to be treated.

Sindoni, A., *Jnr* (1939) *J. Amer. med. Ass.*, **112**, 2503 and 2595.

Treatment

Diet

Binshtok, working at the Clinic of the Institute of Nutrition in Odessa, tried substituting a portion of the fat given in the non-insulin cases of diabetes by carbohydrates. He found that in all these cases an increase of sugar in the urine and in the blood followed such a diet, and therefore gave up this method of treatment. In another series of 27 insulin cases, treated in the clinic for from 30 to 75 days, he tried increasing the quantity of carbohydrates and diminishing the quantity of fat, though he maintained the same number of calories. This treatment was only applied after treatment by insulin and so-called standard diet and when no sugar, or at any rate only traces, were found in the urine, and when the blood-sugar was almost normal. The number of units of insulin administered was unchanged. The patients preferred the increased quantity of carbohydrates, and were more satisfied. After this trial, however, the author found: (i) The substitution of part of the fat by an equal number of calories of carbohydrates causes, in the majority of insulin-treated cases of diabetes mellitus, increase of sugar in both the blood and the urine when the same number of units of insulin are given. (ii) It was not possible even in one case to leave off the insulin either while on a diet with increased quantity of carbohydrates or after this form of diet ended. (iii) The good results obtained by other authors with the application of a diet containing an increased quantity of carbohydrates may be explained by their reaction to the hospital conditions and the administration of insulin. (iv) The tolerance to carbohydrates of diabetics who received an increased quantity of carbohydrates did not increase.

D. Embleton in a paper on the dietetic treatment of diabetes mellitus with special reference to high blood pressure advocated a high protein diet which had been employed for 15 years in about 300 patients, mainly the obese with carbohydrate intolerance. The essential constituents of any meal were: bread 1 oz. only, a minimum of 3 to 4 oz. protein for a male, 2 to 3 oz. for a female, or as much as desired; and a compulsory 4 oz. at least of fruit. This diet was full, satisfying, and provided energy for hard physical exercise. A striking effect was a steady and lasting fall in high blood pressure; it was therefore suitable for cases of hypertension as long as there was not any gross lesion of the kidneys. Many patients with moderately severe diabetes mellitus thus treated became normal, or nearly so, as regards their glucose tolerance curve, and remained so for years. A history of an obese phase was common

in some forms of diabetes mellitus, and might occur in a pre-diabetic state; the obese commonly showed a defective carbohydrate tolerance; this, Embleton found from examination of 500 patients, was present in a very different proportion in the two sexes, namely, 73 per cent of obese males, but only 35 per cent of obese females. A fruit diet, compulsory but unlimited, and exclusively fruit every 2 hours had been found useful in cases of moderate diabetes mellitus; as it might be constipating this tendency must be counteracted. Stress was laid on the importance of 2 good actions of the bowels daily in patients taking the high protein diet. At the present time attention seemed to be concentrated more on improving the general condition of the patient than on attacking the main defect in diabetes mellitus, which was carbohydrate intolerance. The introduction of insulin had led to the neglect of the purely dietetic treatment; patients were too often placed on a so-called high carbohydrate diet, the excess of sugar being met more or less accurately by insulin; this was in many cases followed by marked improvement, less insulin being required and relatively large quantities of carbohydrate being dealt with without much rise in the blood-sugar or glycosuria. Embleton had not seen a case treated on these lines eventually show a normal or nearly normal blood-sugar curve after 50 g. of glucose. The more rational method of treatment was to reduce the glucose tolerance to normal.

W. W. Payne described proferin, a new diabetic flour made from the germ of the carob or locust bean (*Ceratonia siliqua*). Almost completely free from starch this protein, resembling the gluten of wheat in many of its physical properties, could be used in making bread and biscuits, and provided more palatable foods than did the starch-reduced flours hitherto available. In some cases its addition to a diabetic diet had no effect on the blood or urinary sugar; in other cases it slightly increased the glycosuria, but to a less extent than that produced by a corresponding amount of animal protein.

Zinc-Protamine-Insulin

The effects of regular insulin and protamine insulin were compared with regard to their toxicity, dosage, and duration of activity in rats, cats, and rabbits by F. M. Allen. The toxicity of protamine insulin, when large doses were given, was found to be higher than that of regular insulin, as demonstrated by loss of appetite and the deaths of all 3 types of animals. The tolerance of rats, with spontaneous eating, appeared to be less than 60 units of protamine insulin. When fasting, with parenteral glucose injections the rat tolerance is below 15 units. A single dose of 15 units of protamine insulin was almost equivalent to 800 units of regular insulin, given in doses of 100 units at 12-hour intervals, in respect of carbohydrate metabolism. The duration of the hypoglycaemic effect was 120 hours and 124 hours respectively. In rabbits the duration of the hypoglycaemic effect with a dose of 200 units was found to be 8 days. This prolonged duration of protamine insulin is thought to be explained by its slow absorption and, assuming this to be correct, residues from injection may be absorbed for some days, thus explaining the cumulative action of this substance. The only means of attaining the same results with regular insulin is by giving a fraction of a unit and repeating it at short intervals. Glucose consumption, with small doses of protamine insulin and very large doses of regular insulin, appears to be more or less the same, but, in the case of the protamine insulin, toxic symptoms do not manifest themselves. The author performed experiments whereby injections of protamine insulin were given near the ankle and the leg amputated above the knee. It was found that after lethal doses both in rats and rabbits, life could be saved, even when amputation was delayed for long periods. In the case of rats this period was found to be up to 62 hours, during which time glucose was administered. Feeding was found to be difficult in rabbits after large doses of protamine insulin. Crystalline zinc insulin was found to give results midway between regular insulin and protamine insulin, in regard to toxicity and duration of action.

H. O. Mosenthal and M. F. Mark have studied a series of diabetics treated over a period of 6 months with zinc-protamine-insulin alone, and with the addition of regular insulin. The clinical material was derived from three sources: namely, private patients who attended the surgery, hospital out-patients, and in-patients of a tuberculosis institution. It was not considered that tuberculosis affected the diabetic picture except when high or prolonged fever was present, and such cases were not included in this study. The standards adopted with regard to improvement were as follows: Good results were those cases in which less than 1 per cent glycosuria was usually exhibited in no more than one urinary specimen per day. Poor results

were those in which the glycosuria was more pronounced. When excessive glycosuria or severe hypoglycaemic reactions occurred, regular insulin was substituted for zinc-protamine-insulin.

The maximal dosage of zinc insulin was considered to be 40 to 50 units per day, but mild cases were controlled by 20 units or less. If the maximal dosage of zinc-protamine-insulin was insufficient, regular insulin was added. Generally, whether the dose was zinc-protamine-insulin alone or in conjunction with regular insulin, one injection was given in the morning before breakfast (2 needles being used if both types of insulin were given). Two-thirds of the cases reviewed were in this category. One of the advantages of the use of zinc-protamine-insulin was the smaller number of injections required. Occasionally, better results were obtained by giving divided doses morning and evening. It should be remembered that, when ordinary insulin is given with zinc-protamine-insulin it becomes much more potent, and the dosage must be regulated accordingly. The suggested initial dose was 4 to 6 units, raised by 2 units to 12 or 14 once or twice a day. It was considered that hypoglycaemia, which is frequently regarded as a disadvantage in the use of zinc-protamine-insulin, could be controlled by correct dosage and attention to exercise. Patients were advised to consume a certain amount of carbohydrate before attempting any walking or other exercise. Zinc-protamine-insulin appears to be contra-indicated in patients who undertake violent exercise or exertion.

The results obtained in this series with zinc-protamine-insulin, combined if necessary with regular insulin, were summarized as good in 88.6 per cent, and poor in 7.9 per cent, while in 4 cases out of the total of 114 the use of zinc-protamine-insulin was discontinued.

L. A. Chase stated some rules for the use of zinc-protamine-insulin in the treatment of diabetes mellitus. A dose should be given which will cause a fall in the night blood-sugar of not more than 10 mg. per hour from 10 p.m. to 8 a.m. Even if the evening blood-sugar is high no greater dose should be given, as the possibility of greater exercise being taken in the morning may make the morning reaction very unpleasant. If the patient is to be transferred from unmodified insulin to zinc-protamine-insulin, the following rule has been followed. If the total number of units of insulin the patient has been having daily is less than 40, 5 is added and that total number is the initial dose of the zinc-protamine-insulin. In addition the patient receives 5 units of unmodified insulin for 5 days before breakfast. When all tests are sugar-free for 24 hours the dose of zinc-protamine-insulin is reduced by 5 units a day; when the dose gets below 20 units it is reduced by 2 units a day until a positive test for sugar appears, when the reduction is stopped. If the total dose of unmodified insulin is more than 40 units a day, 10 is added to the total, 10 units of unmodified insulin is given before breakfast, and the dose of zinc-protamine-insulin is reduced by 10 units a day when all the tests are sugar free. The dose of 10 unmodified units may or may not be discontinued or may be given at noon. If a new patient is to be treated he is first stabilized on unmodified insulin and then transferred to zinc-protamine-insulin in the above manner.

R. Boller summarized the modern treatment of diabetes mellitus with retard insulins, and pointed out the importance of exact dosage and its control by frequent blood-sugar tests, as retard insulin is still active when the next dose is given, and therefore the second dose should always be slightly less. A late evening meal should be given to shorten the period of abstinence from food, and when changing from ordinary insulin to retard insulin only 60 to 70 per cent of the original units should be given. No patient should be treated from the outset with retard insulin; ordinary insulin should be used for the first few days, and a change-over should be effected after that. Diabetic coma should still be treated with ordinary insulin. The complicated cases in which pulmonary tuberculosis or disturbances of the circulatory system co-exist react very well to retard insulins.

Complications of Insulin Injections

Local induration.—Histamine is liberated in the body not only from injured tissue but also by cellular stimulation. It is destroyed by the enzyme histaminase. Patients with hypersensitiveness to cold may be cured by desensitization with histamine or by detoxification with histaminase from intestinal mucosal extracts. G. M. Roth and E. C. Rynearson applied these findings to patients receiving insulin who develop red, hard, tender, itching lumps, 2 to 6 inches in diameter, lasting several days. These reactions may usually be avoided by using pork or crystalline insulin instead of beef insulin. If this fails, desensitization to insulin by the intradermal method with increasing doses may be tried. The authors treated a resistant case

with desensitizing injections of histamine phosphate commencing with 0.002 mg. and increasing the amount by 0.05 c.cm. at each injection, which was given twice daily. Later the patient was given 3 tablets of histaminase, three times daily. Eight to 10 days of treatment with the latter only were required before the reaction ceased.

Local atrophy.—From a review of the local atrophy of the subcutaneous fat after the injection of insulin for diabetes mellitus H. Blotner concluded that it was commoner in young females than in males. It resulted in depressions, usually permanent, in the skin varying in diameter from 2 to 9 cm. and in depth from 1 to 3 cm. He reported this change in a thin non-diabetic woman after insulin injections for 3 weeks to increase her weight. About 4 to 5 months later atrophy was seen in the right thigh, where the insulin had been injected twice as often as in the left, and increased during the subsequent 4 months. Sensation was diminished over the area of atrophy.

Insulin hypersensitivity.—K. Herzog reported his observations on the phenomenon of insulin hypersensitivity and its treatment by desensitization with protamine insulin, in patients in whom a preliminary test (Kustner-Prausnitz) revealed the allergic nature of the phenomenon. The hypersensitive patient, who reacts both locally and generally or even only locally at the site of the injection, is tested with intracutaneous bovine insulin, bovine serum, physiological saline, and bovine pancreatic extract. The same test is carried out in a healthy control individual. An enlarged wheal at the site of the insulin and/or the pancreatic extract proved the allergic nature of the condition. Desensitization was carried out by highly diluted insulin 1 : 10,000,000 in very sensitive cases; in milder cases a dilution of 1 : 100 was recommended. A small dose of the daily total quantity is given half an hour before injection, which is carried out slowly. The daily pre-injection dose is now increased, and the proper injection accordingly reduced. It was interesting, in the author's view, that the allergic reaction was different in extent in various parts of the body; in one patient the left arm showed a more pronounced reaction than the right. Desensitization sometimes causes transient tachycardia, headache, and nausea. The author advised preliminary testing in all diabetic patients before starting injection treatment.

Peroral Insulin

Many attempts have been made to give insulin, often in very large doses, by mouth; but it is inactivated by pepsin, trypsin, and papain. From experiments on mice H. Wilson *et al.* found that the inactivation of insulin by enzymes *in vitro* may be reversed in whole or in part. About 90 times the subcutaneous dose of undigested insulin hydrochloride or 45 times the subcutaneous dose of digested insulin hydrochloride produced hypoglycaemic convulsions or coma in mice within 2 hours of its administration. The response to oral insulin differed from the response to subcutaneous administration in not being proportional to the dosage. Iron salts increased the effectiveness of insulin and papain digests of insulin when given orally. These observations suggested that under suitable conditions effective oral administration of insulin might be possible.

A further contribution to this problem has been made by F. Lasch and E. Schönbrenner who discussed whether insulin is absorbed at all by the stomach and intestine. Owing to the large size of the insulin molecule, there is a great loss during absorption. The main reason, however, why insulin is not used orally is that it is quickly destroyed by the enzymes of the intestinal tract. The authors had showed previously that certain organic dye-stuffs such as Congo red and trypan red protect insulin against pepsin, and others such as malachite green and rhodamine against trypsin. The authors proceeded to experiment on patients with a combination of saponin, trypan red, malachite green, and dried insulin. None of the components is toxic. By giving 30 units of insulin orally, they reduced the blood-sugar in one case from 80 mg. per 100 c.cm. to 50 mg. per 100 c.cm. in 4 hours, and in another from 150 mg. per 100 c.cm. to 110 mg. per 100 c.cm. after 5 hours. Out of 40 patients some did not react to the peroral insulin (number not stated); in most patients, however, the insulin was effective so far as reduction of blood-sugar, urinary sugar, and body weight were concerned. In one case urinary sugar was eliminated by doses of 90 units per day, and blood-sugar reduced from 210 mg. per 100 c.cm. to 100 mg. per 100 c.cm. Weight was increased from 50 kilos to 51 kilos. In another case urinary sugar disappeared after 6 days' treatment consisting of 150 units twice daily; blood-sugar was reduced from 240 mg. per 100 c.cm. to 170 mg. per 100 c.cm., and weight increased from 67 kilos to 69 kilos. The amount of insulin necessary is about 2 to 4 times as much as that by injection. The effect is not as rapid as by injection,

but persists for 1 to 2 days. The tablets were given one hour before lunch and supper, and immediately after breakfast.

Subcutaneous Implantation of Insulin Tablets

As the prolongation of the action of subcutaneously administered insulin has obvious clinical advantages, as shown by the great value in diabetes mellitus of long-acting protamine-insulin and zinc-protamine-insulin, and as experiments with the sex hormones have shown that many of them, when implanted under the skin in the form of a solid tablet, exert an increased physiological effect and for a longer period (Deaneally and Parkes, 1937, 1938), A. S. Parkes and F. G. Young investigated the possibility of a similar prolongation of the effect on the blood-sugar level in rabbits and of the subcutaneous implantation of tablets of insulin. The experiments were described and discussed in detail, and clearly showed that the hypoglycaemic action of subcutaneously-implanted tablets is only very slightly more prolonged than that of subcutaneously injected solution, when big doses are used.

W. Beckert treated 60 cases of diabetes mellitus with yeast. Mild cases were first put on a suitable diet, and, if after 2 to 3 weeks glycosuria persisted, 40 to 60 g. of yeast were given. In medium and severe cases insulin was administered until, with suitable diet, glycosuria disappeared. Then yeast, in the same quantity as above, was given. The yeast should be taken in amounts of 20 g., 15 minutes after meals, either dry or with a little milk. In 22 of the 60 cases there was a definite improvement after yeast therapy. Glycosuria disappeared and the blood-sugar level was reduced. In 11 cases it was doubtful if the improvement was due to the yeast or to diet. In 25 cases no improvement was observed. The therapeutic effect of yeast can be observed only after at least a fortnight. Sometimes it takes as long as 4 weeks.

Haematoporphyrin

J. Huhnfeld made the remarkable observation that, during the course of treatment of patients suffering from neurosis of the cyclothymic type—depression and melancholic neuroses—with haematoporphyrin, the blood examinations revealed a constant lowering of the level in the blood-sugar. The author tested the effect of haematoporphyrin in the treatment of 10 cases of diabetes mellitus, and found that it had a constant and definite, if only moderate, hypoglycaemic action. Its effect was supposed to be due to its catalytic action. The author suggested a further trial of this treatment. No side-effects were observed.

Surgical

Many measures have been advocated for the surgical cure of diabetes mellitus. P. Ljvruga stated that ligature of the pancreatic ducts and massive ligature of the pancreas have failed to improve the condition. Ligature of the ducts of the salivary glands has also failed, because there is no internal secretion capable of lowering the high blood-sugar, and this operation does not, as some observers have believed, increase the ability of the pancreas to manufacture insulin. Bilateral denervation of the adrenals with the object of weakening the anti-insulin system has been advocated, but results in hypoadrenalism, and in one case death occurred from Addison's disease. Similarly, thyroidectomy results in myxoedema. Denervation of the stem of the liver has also been unsuccessful.

Prognosis of Treated Diabetes

R. D. Lawrence and K. Madders investigated the employment record of 100 diabetics, and found that 77 per cent did not lose any time from their work after the initial stabilization of treatment, and that 55 per cent lost some time from illnesses unconnected with diabetes mellitus. The survey showed that most treated diabetics were good employees from the health point of view, and suggested that their exclusion from government offices, pensionable services, and even private business houses was unfair and nowadays unwarranted.

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Diabetes in Children

Hepatic Enlargement in Children with Severe Diabetes Mellitus

P. White *et al.* contributed 2 papers in succession on hepatomegaly in children with severe, poorly controlled diabetes mellitus; in the first paper, based on 60 cases, the prognostic significance and complications are specially pointed out. The sexes were equally affected. The hepatic enlargement, which might be considerable and reach below the umbilicus, was firm, due to fatty infiltration rather than to glycogen storage. Attacks of acute abdominal pain, in half the cases, which have in 15 instances suggested gall-bladder disease and laparotomy, may be due to stretching of the capsule of the liver. The spleen was enlarged in 31 of the 60 cases. These patients are prone to complications such as coma, ketosis, hypoglycaemia, dwarfism (30 cases), arteriosclerosis, neuritis, and tuberculosis and other infections. As judged by the ordinary tests for hepatic function, 2 cases only showed evidence of inadequacy. The average age of 6 fatal cases was 16.7 years and of 54 living patients 15 years.

In the second paper the effect on the size of the liver was noted after the administration of raw pancreas, betaine hydrochloride, and protamine-insulin. In 2 patients raw pancreas did not exert any effect; 6 out of 12 patients given betaine hydrochloride showed some diminution in the size of the liver, and protamine-insulin produced diminution in 15 out of 19 patients. The decrease in size might occur 2 weeks after the commencement of treatment. This effect was ascribed to the efficient control exerted by protamine-insulin on diabetes mellitus, and it was concluded that hepatic enlargement was not due to the absence of some factor in raw pancreas but because diabetes mellitus, when not properly controlled, caused disorder of fat metabolism.

Endocrine Disorders

P. White investigated the endocrine functions of 1,250 juvenile diabetics in whom the disease had started before the age of 15. The first sign of impending diabetes in children is excessive tallness. This increase in bone activity is due to increase of pituitary activity, but this activity may later become subnormal and result in pituitary dwarfism. Dwarfism was seen in 59 out of 94 patients. The dwarfism commonly occurs 4 to 5 years after the onset of the diabetes. These patients can be treated with diet, thyroid, or pituitary extract, the last producing the most dramatic results.

Deficiency of the posterior lobe of the pituitary occurred only once in this series, and was manifested by a temporary diabetes insipidus. Hyperactivity of the adrenal cortex has been associated with adult diabetes but no evidence of it was found in these children. Three of the patients had typical primary hyperthyroidism accompanying their severe diabetes; the former was decreased by operation on the thyroid gland. There were no cases of myxoedema or cretinism. Menstruation and gonadal activities were found to have little influence on the diabetes. The chief antenatal accident found by White was asphyxia neonatorum which appeared to have no direct relation to the level of the blood-sugar. Oestrogen has been given to diabetic patients with favourable results. Two of the 1,250 juvenile patients showed evidence of hyperinsulinism along with the diabetes. One patient with a mild border-line condition required no treatment with insulin while another showed a diabetic condition for approximately one of every 24 hours but she had to be given frequent small carbohydrate feeds or spontaneous hypoglycaemia developed. The cause of this condition was unknown but adenoma of the islets of Langerhans, pituitary

insufficiency, and the enlarged liver causing improvement in the diabetes were suggested.

Treatment

F. Linneweh and M. Eitel experimented with retard insulin in infantile diabetes mellitus. The difficulties in the treatment of diabetic children were that they required a normal diet for their development and that they were far more 'insulin sensitive' than adults. Many children had to be left with a slight glycosuria to prevent the development of hypoglycaemic symptoms. When ordinary insulin was used, the blood-sugar curve showed sudden rises and falls; with retard insulin it was smoothed out. Children treated with the usual insulin, when given even a slightly increased amount of carbohydrate in their diet, showed an abnormal increase of blood-sugar and glycosuria; but in children treated with retard insulin a small increase of carbohydrate did not markedly change the blood-sugar curve.

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White, P., (1939) *Arch. intern. Med.*, **63**, 39.

— Marble, A., Bogan, I. K., and Smith, R. M. (1938) *ibid.*, **62**, 740, 751.

Diabetic Coma

Treatment

Sodium bicarbonate.—E. Kirk, of the Medical Clinic of the University of Copenhagen, advocated the intravenous administration of isotonic (1.3 per cent) solution of sodium bicarbonate as an excellent and safe remedy for the relief of diabetic coma with acidosis, when insulin was slow in its action. Of recent years this old treatment of diabetic coma had been little used, as it was superfluous because insulin was so effective. In some cases, however, the action of insulin was so slow that it was desirable or even imperative to neutralize the ketosis by other means. Kirk reported 2 cases of diabetic coma with severe ketosis in which insulin did not bring about the expected improvement. The intravenous injection of the bicarbonate solution was followed by a dramatic and immediate recovery. In this treatment it was generally necessary to determine the plasma bicarbonate values several times during the first 24 hours. When it was impossible to make these determinations, not more than 2 litres of the isotonic bicarbonate solution should be administered at the commencement.

Kirk, E. (1939) *Lancet*, **1**, 505.

Factors Complicating Treatment

Pulmonary Tuberculosis

A. M. Recardier discussed the influence of insulin treatment on pulmonary tuberculosis in the course of diabetes mellitus. Running parallel with the prolongation of life and the fall of deaths from coma in diabetes mellitus due to insulin there had been an increase in the death-rate due to pulmonary tuberculosis among diabetic patients, and in children as well as in adults. The morbid changes in the lungs and the clinical features of pulmonary tuberculosis in diabetes mellitus had undergone modifications. In the pre-insulin era the lung lesions were rapid, extensive, and predominantly caseating; now they were slower and more fibrotic, and the evolution of the tuberculous process was delayed; this was correlated with diminished activity of allergy in diabetes mellitus. Clinically, fever was absent in 15 per cent, and wasting present in 60 per cent and severe in 40 per cent of the author's patients. The combination of the treatment of diabetes mellitus by insulin and the complication of pulmonary tuberculosis by collapse has given encouraging results.

Pregnancy

F. S. Smyth and M. B. Olney state that, since 1922, 19 infants have been born of women whose pregnancies were complicated by diabetes mellitus. In 14 of the mothers glycosuria appeared only with gestation and was controlled by diet or by diet and the temporary use of insulin, thus suggesting that it was due to causes other than diabetes mellitus. Of the entire group, 11 gave birth to excessively large infants. One mother had had 9 children: one, in her first marriage, was of normal weight; the other 8, in 2 subsequent marriages, all weighed 10 pounds or more at birth. This has been ascribed to the increased nutrition provided by the raised maternal blood-sugar. The newly-born infants of diabetic mothers demand special care, not only because of the insulin given just before delivery, but also because of the

possibility of essential hyperinsulinism as reported by S. H. Gray and L. G. Feemster. The authors specially investigated infants born of diabetic mothers in the last few years, particularly as regards the blood-sugar estimations of the mother, the cord, and the infant. Accounts of changes found after death in the infants born of diabetic mothers vary; in some there was not any hyperplasia of the islets of Langerhans found, and the hypoglycaemia may be considered functional; but in others this change was present, and the correlation with hypoglycaemia is obvious. The authors concluded that, under rigid control, the diabetic woman may pass satisfactorily through pregnancy, and that her infant may be healthy. Although reports vary, it is difficult to prove that the infantile production of insulin exerts a compensatory effect on the maternal blood-sugar. When the maternal diabetes has not been adequately controlled, the new-born infants may present temporary symptoms referable to hypoglycaemia. In some cases these symptoms of cyanosis, vomiting, and feeding difficulty may persist for as long as 3 weeks and necessitate parenteral glucose administration for that time. A follow-up of one patient showed a hyperinsulin-like sugar curve at 4 years of age.

Alkalosis

C. W. Erickson and E. J. Kepler reported a case of severe diabetic ketosis and superimposed alkalosis, self-induced by a man aged 42 known to have been the subject of diabetes mellitus since 1918. Some 15 days before admission to hospital the diabetic symptoms became aggravated, he ceased injecting insulin, and during the 20 hours before admission he took 250 g. of sodium bicarbonate. On admission to hospital in a drowsy, dehydrated state he was breathing shallowly and regularly at a rate of 18 to 20 a minute, without any evidence of tetany.

Treatment consisted in combating 2 main factors, (i) the diabetic ketosis with the attending dehydration and loss of chlorides and (ii) reduction of the high alkaline reserve, without increasing the high level of the total base and the elevated pH of the serum. There was never any evidence of renal damage. Sodium chloride was given intravenously as physiological saline for the first 3 days, but it became obvious that the intake of sodium should be reduced, and accordingly ammonium chloride was given by the mouth. The intake of fluid varied between 2 and 3 litres daily. Gastric lavage was carried out on the second day to control vomiting; there was no free hydrochloric acid; 5 c cm. of water, containing 20 minims of dilute hydrochloric acid, were instilled into the stomach, and the nausea ceased. Two days later the patient was capable of taking a full diabetic diet.

Diabetes Insipidus

D. I. Rutledge and E. H. Rynearson reported a case of the coexistence of diabetes mellitus and diabetes insipidus; in an obese woman, aged 56, the symptoms of polyuria and thirst followed glycosuria, but were relieved by the nasal insufflation of powdered pituitary, a method of treatment they described in another case of diabetes insipidus. The combination of the two forms of diabetes is rare, and reference was made to the paper on this subject in which J. A. Greene and R. B. Gibson collected 20 recorded cases.

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DIAPHRAGM DISEASES

See also Vol. III, p. 673.

Congenital Diaphragmatic Hernia

Clinical Picture

K. A. Meyer *et al.* lay stress on the importance of the early diagnosis and operative treatment of diaphragmatic hernia. In the new-born, cyanosis and disturbances of the cardio-respiratory mechanism are the main symptoms. Difficulty in feeding,

vomiting, and loss of weight may occur. A peculiar weak cry has been observed. Physical signs are rare in the new-born, but tympanites of the involved side, absence of breath sounds, dullness on percussion of the other side, bulging of the thorax, gurgling sounds in the chest, or retraction of the abdomen may rarely occur. In older children vague dyspepsia may be added to the symptoms. If the condition is suspected X-ray examination should be made after a barium sulphate meal. The treatment is surgical. One of the youngest patients in whom operation has been successful, namely. 13 days after birth, is reported.

Meyer, K. A., Hoffman, S. J., and Amtman, J. K. (1938) *Amer. J. Dis. Child.*, **56**, 600.

Primary Rhabdomyosarcoma

T. M. Peery and W. A. Smith recorded a primary rhabdomyosarcoma of the diaphragm in a negro boy, aged 14 years, who had pain and a frequently recurring pleural effusion on the right side, where a tumour was shown radiologically. The tumour had spread by the lymphatics against the stream to the retroperitoneal lymphatic glands and to those above the right clavicle. This case brought the number of primary tumours of the diaphragm up to 10, of which 6 were malignant, another being a rhabdomyosarcoma, and another a leiomyosarcoma.

Peery, T. M., and Smith, W. A. (1939) *Amer. J. Cancer*, **35**, 416.

DIARRHOEA ASSOCIATED WITH FLAGELLATE INFECTION

See also Vol. IV, p. 12.

Giardia Intestinalis

Treatment

A. Cade and M. Milhaud examined the modern treatment of intestinal lamblasis, which causes chronic inflammations of the small intestine, abscess formation, and marasmus, and often co-exists with intestinal tuberculosis and amoebiasis. Quinacrine (a derivative of acridine) was found useful in the treatment of the condition; 0.1 g. 3 times daily was given for the first 5 days, after which a few days' pause was observed, and then a second, third, or further series followed. Stovarsol injections were also given, 0.5 g. over 8 days, and bismuth carbonate was regularly administered in conjunction with chologagic preparations.

Cade, A., and Milhaud, M. (1938) *J. Méd. Lyon.*, **19**, 485.

DIARRHOEA IN INFANCY AND CHILDHOOD

See also Vol. IV, p. 21.

Treatment

Raw Apple and Tea

W. Sheldon and M. Hall treated with raw apple pulp and weak tea 36 infants suffering from diarrhoea of varied aetiology. The tea was included to provide greater fluid intake, and was found for this purpose to be better than water. Most of the infants had been suffering from diarrhoea for at least a week before treatment began, and had been passing 4, 5, or more curdled, green, offensive stools a day. Soft juicy apples were used. They were pulped and fed as a mash, and the peel was not included as, even when finely cut, it made the patients vomit. Feeds, either with a spoon or with a bottle with a large-holed teat, were given 3-hourly throughout the day and night. For children under one year of age, one teaspoonful was given in every feed, and over one year of age the pulp of the whole apple was given. In patients fed from a spoon the treatment was stopped after 72 hours; in those fed from a bottle it was continued for 4 days, because the pulp had to be diluted with water.

The large majority of the patients recovered from the diarrhoea, and gained weight. The toxæmia was lessened under the treatment, and the stools improved in character. This treatment was of special value for infants suffering from persistent

diarrhoea associated with loose offensive motions. The success of the treatment is thought to be due to the pectin contained in apples, which acts as a colloid and prevents the absorption of toxic products. Another hypothesis is that the tannic acid compounds present in the apple act as an astringent. All the patients in this series developed brown patches on the tongue and buccal mucosa which may have been due to the astringent effect. Another hypothesis attributes the action of the apple in stopping the diarrhoea to the malic acid which it contains.

Sheldon, W., and Hall, M. (1939) *Arch. Dis. Childh.*, **14**, 43.

DIET IN TREATMENT

See also Vol. IV, p. 38.

Fasting

H. E. Meyer and H. Bottenberg reported on fasting, its logic and its practice. In the first days of fasting there is increased excretion of nitrogen. Hypertensive patients excrete a large quantity of xanthoproteins. Between the fifth and the tenth day of fasting increased amounts of acetone are found. In acute and chronic infective arthritis, muscular and joint rheumatism, arthropathia deformans, chronic dyspepsia, colitis, intestinal auto-intoxications, and diseases of the circulatory system, fasting is an advisable supplement to treatment. The patient must remain under the observation of the physician. Tea and fruit juice should be given in sufficient quantities to quench the thirst, and the bowels must be opened by enemas if they do not open regularly. In less rigorous cures fruit and vegetables are allowed in small quantities. It is important to maintain the vitamin administration during fasting.

Meyer, H. E., and Bottenberg, H. (1939) *Med. Klinik*, **35**, 896.

Effect of Cranberries on Calcium Retention

Animal experimentation by A. Mindell *et al.* showed that addition of 20 per cent fresh cranberries in an adequate diet for white rats, increased body calcium retention 8.4 ± 0.8 per cent, while under similar conditions apples increased body calcium retention 10.8 ± 1.1 per cent. The calcium content of the femur was slightly increased by administration of cranberries, but was practically unaffected by apples. It was considered that the increased acidity of the intestinal tract was probably the cause of increased calcium retention, or that the acid of the fruit may have reacted with the calcium carbonate in the diet to produce calcium salts more soluble than calcium carbonate.

Mindell, A., Esselen, W. B., Jr., and Fellers, C. R. (1939) *Amer. J. digest. Dis.*, **6**, 116.

DIETETIC DEFICIENCY DISEASES

See also Vol. IV, p. 51.

Deficiencies in Relation to Disease

Dermatological Manifestations

H. Goodman described the dermatological manifestations which may occur in vitamin deficiencies. His observations were based on the study of clinical and animal conditions. He divided the hypovitaminoses into 3 types: (i) the true hypovitaminoses in which the skin manifestations are essentially part of the vitamin deficiency diseases as in scurvy and pellagra, (ii) the relative hypovitaminoses in which skin manifestations accompany the vitamin deficiency disease, but the factor of the vitamin responsible for them is unknown, and (iii) paravitaminoses in which the lack of vitamins is only a secondary cause of a distinct pathological skin condition. This occurs in certain types of eczema.

Lack of vitamin A gives rise to many skin conditions. Among these are xerophthalmia, redness and harshness of the skin, brittleness of the nails, papular eruptions, increased keratinization, atrophy of the sebaceous glands, impaired function of the sweat glands, and falling of the hair. Lack of vitamin B₁ produces cutaneous lesions in polyneuritis, burning of the soles of the feet, and acrodynia. Vitamin B₁

has been successfully administered in the treatment of herpes labialis, herpetic stomatitis, and other diseases of the mucosa. Lack of vitamin B₂ produces the skin lesions of pellagra, and loss of hair in experimental animals. Lack of vitamin C produces the ecchymoses, stomatitis, and loss of hair typical of scurvy. Vitamin C has also been used in the treatment of psoriasis and herpes. The role of vitamin D in diseases of the skin has not yet been determined, but it has been administered with success in many lesions, among them pemphigus and acne. Lack of vitamin D causes rats to lose their hair. Vitamin E has cured a disease of the hair in rats. Vitamin F is said to prevent scaly skin on the rat's tail, and other lesions similar to seborrhoea.

Goodman, H. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 389.

DIPHTHERIA

See also Vol. IV, p. 72; Cumulative Supplement, Key No. 324; and pp. 41 and 74 of this volume.

Bacteriology

H. Wilson and N. E. Goldsworthy isolated 200 strains of *Corynebacterium diphtheriae* from 325 patients. A hundred and nine were infected by type *gravis*, 13 by type *intermedius*, 47 by type *mitis*, and 31 by atypical strains. The first group contained 5 deaths; the second one death and the third also one death. Most antitoxin was given to patients infected by type *intermedius*, which suggests that disease due to this type is more severe than that due to the other types. Of the 23 cases of malignant diphtheria, 13 (56·5 per cent) died. It is shown that in this condition even large doses of antitoxin are not effective. The authors are of opinion that the Claiberg medium has shown more positives than Loeffler's medium in the recognition of *C. diphtheriae*. The blood-agar medium renders distinguishable after 18 hours the colonies of type *intermedius* and the colonies of *gravis* from *mitis*.

Wilson, H., and Goldsworthy, N. E. (1938) *Med. J. Aust.*, **2**, 509.

Complications

Prognostic Importance of Albuminuria

O. Künzel stated that some authors do not attach any importance to diphtheritic albuminuria, whereas others regard it as a good indication of intoxication. The author examined 558 cases with a view to determining the true prognostic importance of the condition. He found that all the patients who died of the disease showed an albuminuria of up to 7 per thousand. Patients who had an albuminuria of more than 0·25 per thousand during the second and third day of the disease soon had serious complications. The total number of deaths was 34 (6 per cent); 174 cases (31 per cent) showed albuminuria. If the albuminuria was very slight and lasted only 2 to 5 days, there were as a rule no complications. If the albuminuria increased and lasted for more than 5 days, then complications occurred (myocarditis, paresis of accommodation). Serum injections did not in any way influence the excretion of albumin in the urine.

Künzel, O. (1939) *Dtsch. med. Wschr.*, **65**, 328.

Diagnosis

Potassium Tellurite Test

E. Tomlin investigated the claims made by Manzullo regarding the possibility of bedside diagnosis of cases of diphtheria with pharyngeal exudate by his potassium tellurite test, the figure of accuracy which is claimed for the process being 96 per cent. The solution of potassium tellurite in distilled water had a strength of 2 per cent. Care was taken to avoid heating it above 40° C. and the solution was not used after being kept for a month. It was applied to throat exudates by means of a swab, contact with the tongue being carefully avoided. Between 5 and 10 minutes later, the throat was examined, and revealed in many cases definite darkening of the exudate.

This test was carried out by Tomlin in 46 cases, 44 being admitted to hospital as

diphtheria or suspected diphtheria. Of these, only 28 turned out to be positive. Of the original 44, 15 were diagnosed as not being diphtheria on bacteriological and clinical grounds in spite of the fact that 9 showed darkening—an unexpectedly high proportion of false results. One case was diagnosed clinically as diphtheria though bacteriologically it was negative.

These figures suggest that, although with a negative result one is justified in assuming that the case is not one of diphtheria, a correct diagnosis cannot be made when employing this test owing to the high number of positive false results obtained. The disparity between these figures of Tomlin and those of Manzullo may be due to the fact that organisms which give darkening are epidemic, and may be present in exudates in sufficient numerical strength to give darkening with the test, even though they are not the causal organisms.

The tellurite contact test was investigated also by J. B. L. Tombleson and R. M. Campbell who compared it with the results of bacteriological investigation and clinical diagnosis of diphtheria. As they found that more than one application of tellurite was necessary in some cases before a positive result could be obtained, in many cases they substituted 40 per cent glycerin in distilled water. Definite blackening of the membrane occurred in 85 per cent of cases of diphtheria, but also in 47 per cent of non-diphtheritic faucial conditions, such as tonsillitis, scarlet fever, and Vincent's angina. A small number of cases of severe diphtheria did not furnish positive results and the test was usually not very helpful in the nasopharyngeal type. The authors think that, though it is of some value, the chances of a wide margin of error are too great for the method to replace clinical diagnosis.

Cutaneous Scratch Test

A cutaneous scratch test for diphtheria has been devised by M. Grozin. It has the advantages that it is quick, sensitive, and requires no syringes and needles. Toxin containing 30 flocculating units per c.cm. was used, originally in the strength 1,200 minimal lethal doses per c.cm. Two drops of the toxin were placed on the skin of the forearm 3 inches apart, and the skin under and between them was scarified. The toxin was then rubbed in, and the scratched area between the drops formed a control. A positive result consisted in the formation of a papule after 48 hours with a pustule and crust in the centre: on the fourth day the pustule dried up, by the sixth day the crust disappeared, and by the eighth to the fifteenth day all traces of the reaction vanished. One hundred children were tested and simultaneously Schick-tested, and there was complete agreement between the 2 tests in 92 per cent of cases. The test is specific and is analogous to von Pirquet's test for tuberculosis. Both are performed and read in the same way, and both have an incubation period of 2 to 4 days.

Grozin, M. (1939) *Amer. J. Dis. Child.*, **57**, 564.

Tombleson, J. B. L., and Campbell, R. M. (1939) *Brit. med. J.*, **1**, 1275.

Tomlin, E. (1939) *Brit. med. J.*, **1**, 1273.

Treatment

Antitoxin Therapy

The relative values of natural antitoxin (whole serum) and concentrated serum (globulin only) are contrasted by B. A. Peters to discover whether, in the process of concentration, the antitoxin loses any of its therapeutic efficiency. The cases selected were considered by the medical officer on admission to be so gravely ill as to need a large intravenous injection of antitoxin (usually 30,000 units) and 60 to 100 c.cm. of 20 per cent glucose, together with 16,000 units intramuscularly. When administered intravenously (i) the therapeutic effects of natural and concentrated diphtheria antitoxin on the death-rate and paralytic complications are equal; and (ii) concentrated antitoxin is 20 times as likely to give severe immediate reactions and one and a half times as likely to give late serum rashes as whole natural antitoxin. As a result the author has decided to use natural diphtheria antitoxin for intravenous injection, and to reserve concentrated serum for intramuscular injection in milder cases.

Among 200 patients treated at the Belvidere Hospital, Glasgow, with refined diphtheria antitoxin (Pope), A. Hutchison reported the death-rate as 2.5 per cent only. This antitoxin is prepared by a process of enzyme disaggregation followed by differential heating; the antitoxin-containing molecule is much smaller than in ordinary concentrated serum. Serum rashes were recorded and immediate reactions

after intravenous injection were few. The small bulk of the serum caused less discomfort to the patient than the ordinary concentrated serum. Chewing-gum was useful in adenitis, apparently from the massage of the cervical glands effected by the movements of the jaw in chewing.

Hutchison, A. (1939) *Brit. med. J.*, **1**, 384.

Peters, B. A. (1938) *Brit. med. J.*, **2**, 344.

DISLOCATIONS, FRACTURES, FRACTURE-DISLOCATIONS, AND ASSOCIATED INJURIES

See also Vol. IV, p. 113, and Cumulative Supplement, Key Nos. 326-353.

Delayed Calcification and Atrophy of Bones

Treatment

Hydrochloric acid.—N. W. Cornell *et al.* investigated the cause of atrophy and delayed calcification around the site of fractures in bones. They studied 5 cases in which the local conditions were satisfactory and the patients had a proper diet, good hygiene, and were free from debilitating disease. They presumed that the disturbance was in the absorption and utilization of the calcium, and found reduced gastric acidity and decrease in the volume of gastric contents in these cases. The addition of 4 to 8 c.cm. of 10 per cent hydrochloric acid 3 times a day to a diet high in calcium and vitamins increased absorption of calcium and the calcification of the bone.

Cornell, N. W., Bernheim, A. R., and Person, E. C. (1939) *J. Bone Jt Surg.*, **21**, 40.

Recurring Luxations of Temporo-Mandibular Joint

Treatment

M. Brehant worked out a new operative method for dealing with recurring luxations of the temporo-mandibular joint, which were usually accompanied by creaking and not inconsiderable pain and disability. With a Gigli saw, under local anaesthesia, a small transverse portion of the zygoma near the temporal joint was resected and reinforced with a tibial graft. All other methods, as for instance capsulorrhaphy, showed a number of unsuccessful results; this new method, however, though only tried out in 7 cases, was found to be superior to all previous operative interventions in the treatment of this condition.

Brehant, M. (1939) *Mém. Acad. Chir.*, **65**, 893.

Dislocation of Hip-Joint

Treatment

M. Lange insisted on the importance of plastic restoration of the acetabulum in congenital and acquired dislocation of the hip in order to obtain a permanently good result after the dislocated hip-joint has been reduced; otherwise the dislocation might recur. A technique slightly different from that of Spitzzy and Lance was adopted. In older children 2 bony chips were inserted just above the acetabulum, and the plaster of Paris was kept in position for 4 to 8 weeks. A plastic operation was indicated (i) in children if during the first few years after bloodless reduction of the dislocation a satisfactory acetabulum had not formed spontaneously; (ii) in children in whom immediately after the bloodless reduction dislocation recurred; and (iii) in adults with untreated or unsuccessfully treated dislocations. The first group of patients gave the best results with the plastic operation. In the second group (re-dislocation), the subluxation must be treated first by extension before the operation, or by extension-traction on the operating table. The leg must be extended again after the operation if necessary. In cases of complete dislocation, the joint must be set surgically and plastic operation performed at once. In adults in whom a new acetabulum had formed in an unsatisfactory position, no real plastic operation could be undertaken. The bony chips serve only to increase the hold of the femur, and this was not sufficient. The head of the femur should be

kept in position by a subtrochanteric osteotomy and transplantation of the vastus externus muscle upon the gluteus minor muscle.

Lange, M. (1938) *Munch. med. Wschr.*, **86**, 1823.

Fractures of Upper End of Tibia and Fibula

Treatment

J. Creyssel *et al.* described their method of treating triangular fractures of the head of the tibia. Compound fractures must be excluded from their treatment, which is mainly designed to combine the advantages of open and closed fracture treatment of the triangular fractures of the head without fragmentation. Under local or spinal anaesthesia two small corresponding incisions are made on both sides of the tibial condyles. A pin of 2 mm. diameter is passed through under radiological control and is held in its correct transverse position by a hard rubber ring on both sides of the bone. This rubber ring is pliable so as to prevent tissue damage, and to enable perfect fitting to the bone. A Kirschner wire is passed through the calcaneus, and traction with a 3 to 5 kg. weight is maintained, the limb being placed on a Braun's frame. The authors contended that, with this treatment, the very difficult triangular fractures were at last adequately controlled. The Kirschner wire is passed through 2 or 3 days before the pin in those cases in which anatomical reduction has to be effected owing to more marked displacement. The pin is left in position for about 3 months.

Creyssel, J., Bérard, M., and Dargent, M. (1939) *J. Chir., Paris*, **53**, 758.

Gross Injuries with Fracture of Joints

Treatment

M. Arnaud *et al.*, members of a French ambulance team treating refugee soldiers from the Spanish Civil War, have collected their data and conclusions on the treatment of gross injuries of the limbs complicated by fractures. The fact that the soldiers were in constant retreat made a satisfactory early treatment impossible, and therefore Orr's method of plastering the limbs after reduction of greatly displaced fractures was practised. The authors found that the results were not too good, as early healing was prevented, but on the other hand the method fully justified its use under the very trying circumstances in which the patients found themselves. Very few cases developed septicaemia or other less serious complications, but healing was much retarded and movements were rather limited.

Arnaud, M., Perves, J., Caire, A., and Morvan, F. (1939) *Mém. Acad. Chir.*, **65**, 801.

Fractures of Os Calcis

Treatment

W. Ehalt discussed the present treatment of fractures of the os calcis. Böhler classified calcaneal fractures into 6 groups according to severity and displacement. The fundamental principle of treatment of calcaneal fractures is the restitution of the original form of the bone, as otherwise a constant disability is bound to result; this disability is characterized by pain on walking, pes planus, and irreparable relaxation of the arches of the foot. In Böhler's clinic reduction of displaced fragments is attempted immediately, instead of waiting 8 or 10 days as was formerly advocated. Early reduction, while the fragments are easily movable in the haematoma, allows the use of local anaesthesia, and is a less complicated operation. Transfixation by wire is abandoned, as decalcification is often very marked, and Böhler's nail is introduced from one side only. No plaster of Paris is applied, and the proximal muscles of the leg are massaged every day; after 6 to 8 weeks the patient can stand on his leg again and start to walk. The American method of immediate arthrodesis should not be followed, as it results in recurrence of disability after a shorter or longer interval. If, however, pain reappears in the articulations of the calcaneus, arthrodesis should be performed. Fractures of the calcaneus without displacement need a plaster, but no manipulation.

Ehalt, W. (1939) *Wien. klin. Wschr.*, **52**, 429.

DISSEMINATED SCLEROSIS

See also Vol. IV, p. 187, and Cumulative Supplement, Key No. 354.

Course and Prognosis

M. R. Brown and T. J. Putnam studied 133 cases of disseminated sclerosis, 95 hospital patients and 38 private patients, during an average period of 9 years. During this time, 239 instances of improvement were recorded in 92 of the patients, but in 41 the disease was stationary or progressive. The ambulatory patients in private practice ran a significantly longer and milder course, with more remissions than those in hospital practice. Symptoms due to small lesions, for example diplopia, scotoma, or sensory upset in one limb, tended to regress within a few months, whereas symptoms due to major lesions, such as paraplegia, ataxy, and mental deterioration, were usually permanent. Isolated symptoms disappeared more often than the same symptoms occurring in conjunction with others, and the same applied to first symptoms. It was suggested that, in the acute phase of the disease, the breakdown of the myelin sheath was not necessarily permanent and that, if the associated vascular lesions healed, the axis cylinders functioned once more to a greater or less degree.

Brown, M. R., and Putnam, T. J. (1939) *Arch. Neurol. Psychiat.*, Chicago, **41**, 913.

Diagnosis

From Disseminated Encephalo-Myelitis

The relation of disseminated encephalo-myelitis to disseminated sclerosis has not been definitely settled. The cases examined microscopically in which acute exacerbation of clinical symptoms came on in the course of typical multiple sclerosis seem to be of special value. Three cases were examined by A. Yuba. The first was a woman of 52. She had had a stroke 3 years before; hemiplegia had lasted a very short time only. She died 13 days after a second stroke producing hemiplegia of the right limbs and disturbance of speech. The second case, a woman of 38 years, had suffered 10 years previously from diplopia lasting 2 weeks; she had had paralysis of her right and left limbs 3 years before; she was completely cured, but recently she felt pain in her head and neck, and both lower limbs became paralysed. She died after 17 days. The third case was a man of 37 years; 8 years previously he had had difficulty in micturition. Later, his gait became affected, and for 5 years he could not move his lower limbs. When he was taken into hospital spastic paresis was observed in his limbs; suddenly the paresis became flaccid, reflexes became abolished, and hypotonia was observed. On microscopical examination in these 3 cases, areas of glial tissue were observed round the vessels, at first in the white matter. These areas resembled cases of disseminated encephalo-myelitis. These areas had a tendency to penetrate into the parenchyma and their borders were definite; signs of inflammation were present. From these observations the author concludes that certain severe cases of disseminated sclerosis look absolutely like cases of disseminated encephalo-myelitis, whereas other cases of the same type have nothing to do with disseminated sclerosis. It was observed that the areas of multiple sclerosis arise by inflammation in the neighbourhood of vessels. The author does not believe, as maintained by Putnam, that the areas of multiple sclerosis originate by thrombosis of veins and disturbance of blood circulation produced by thrombosis.

Yuba, A. (1939) *Arch. Psychiat. Nervenkr.*, **109**, 727.

DIVERTICULOSIS AND DIVERTICULITIS

See also Vol. IV, p. 207, and Cumulative Supplement, Key No. 355.

Aetiology

In a series of 3,660 necropsies carried out between 1920 and 1937, J. B. Cleland found that the approximate incidence of diverticula of the colon in adults is probably about 2.5 per cent. The condition was found to be not uncommon in the fifties and tended to develop with advancing years. In the majority of cases the diverticula

were quiescent, but in 6 out of 56 cases rupture of the diverticula had taken place with the development of peritonitis. A seventh died from faecal abscess and gas gangrene. Of the 50 cases of carcinoma of the colon in the total series only 2 were associated with diverticulosis.

Cleland, J. B. (1939) *Med. J. Aust.*, **1**, 70.

Clinical Picture

C. B. Blackburn accepts the distinction between the presence of diverticula (diverticulosis) and inflammation of these diverticula (diverticulitis). The former condition is stated to be present in from 5 to 10 per cent of all persons over 40 years of age, but presents no symptoms, and is usually only diagnosed by radiological examination for some other concurrent condition. Diverticula are most frequently found in the sigmoid flexure of the colon and in the descending colon. They infrequently go on to diverticulitis. The symptoms associated with diverticulitis include pain in the lower left quadrant of the abdomen, either constipation or frequent small relaxed stools, flatulence, malaise, and some rise in temperature. X-rays show the lumen of the involved area encroached on by the swollen mucosa, which may cause sudden obstruction.

Blackburn, C. B. (1938) *Med. J. Aust.*, **2**, 405.

Diverticulum of Duodenum

D. Wheeler divided diverticula of the duodenum into 2 groups. (i) In primary diverticula the wall is formed by the mucous and submucous coats; these are found in the second, third, and fourth parts of the duodenum, and have no obvious cause; they are often multiple and are found most often in the second part of the duodenum on the inside of the loop, and in relation to the head of the pancreas. They vary in size from a pea to a walnut, and are commonest after 50 years of age. They can be divided into (a) those lying in front of the pancreas and covered with peritoneum; (b) those lying in the pancreas; and (c) those lying behind the pancreas. The origin of these mucosal herniations is disputed. Some hold that they are acquired, when they may be traction or pulsion diverticula, but the most popular theory is that they are congenital in origin. Supporting this theory is the fact that they are often accompanied by diverticula in other parts of the gastro-intestinal tract. There are usually no morbid changes in the diverticula, and they give rise to no symptoms unless they become inflamed. They are best diagnosed by X-ray examination. If found and thought to account for symptoms, medical treatment by postural drainage, and intestinal disinfectants should be instituted. If this fails, surgical removal may be undertaken. Wheeler reported a large diverticulum on the outer side of the second part of the duodenum presumably due to trauma incurred at an operation for removal of the gall-bladder. (ii) Secondary diverticula have an obvious cause; in these all the elements of the duodenal wall are present and they occur only in the first part of the duodenum. Various authorities have found different incidences of the condition. On examination of cadavers an incidence as high as 11.3 per cent has been found. On X-ray examination, when the patients are usually younger and the diverticula more difficult to detect, Ayderman found an incidence of 5.19 per cent. Secondary diverticula result from scarring and contraction due to an ulcer with pouch formation. The pouch is the diverticulum. The scarring causes obstruction at the duodenal cap, and thus causes the proximal part to dilate and form a pouch. The morbid anatomy and treatment are that of the underlying condition.

Wheeler, D. (1938) *Canad. med. Ass. J.*, **39**, 214.

Duodeno-Jejunal Diverticula

Two cases of this rare diverticulum at the duodeno-jejunal flexure were published by R. W. Raven. A striking feature is pain in the epigastrium running up to the left shoulder which may come on 1 to 3 hours after food, and disturbs sleep at night. Vomiting may be so incessant as to suggest stenosis of the pylorus. Heartburn and flatulence are often prominent and there is usually some loss of weight. A radiograph after a barium sulphate meal shows the diverticulum passing inwards, upwards, and to the right and lying below the lower border of the body of the pancreas. Complications include: (i) inflammation, which may be sufficiently severe to cause

acute intestinal obstruction; (ii) sepsis in the diverticulum causing duodenitis, pancreatitis, and cholangitis; and (iii) the late formation of an enterolith the weight of which may, by traction and angulation, cause obstruction. If the diagnosis is clear, surgical excision is advisable.

Raven, R. W. (1939) *Lancet*, 1, 203.

Diagnosis

Radiography

Using a contrast medium diverticula show radiographically as oval or rounded, sometimes sessile, sometimes pedunculated projections from the opaque shadow of the bowel. Although, according to H. R. Sear, they may be revealed by either a barium meal or enema, he advocates the use of the enema as the surer method which can also be used to exclude the presence of carcinoma.

From a study of the results of X-ray examination, uncomplicated diverticula appear to be common, and obvious diverticulitis much more rare. In some cases a pre-diverticular state is shown, in the form of small serrations grouped close together along the sigmoid and descending colon.

Differentiation from carcinoma is sometimes radiologically impossible, but usually defects due to malignant disease are more limited in length, show a characteristic lumpiness, and have more even margins. Carcinoma developing in diverticula is rare.

Sear, H. R. (1938) *Med. J. Aust.*, 2, 409.

Prognosis

Discussing the end results of diverticulitis, J. P. Lockhart-Mummery analyses 136 cases of the more serious type, 91 of which were treated by operation and 45 without. Diverticulitis is progressive when not operated on. The mortality directly attributable to this condition was just over 10 per cent for the whole series. He considers colostomy is the safest and most satisfactory treatment for serious cases; 38 colostomies were performed; 4 patients died and 34 have survived for long periods without symptoms. Resection, if postponed until a year after colostomy, is the ideal treatment when the area of the affected bowel is small. Pericolic abscesses are difficult to treat, but drainage and colostomy well above the affected area is the only possible treatment. In 5 patients treated by appendicostomy, the attacks have ceased and health is good in all but one.

Lockhart-Mummery, J. P. (1938) *Lancet*, 2, 1401.

DRUG ADDICTION

See also Vol. IV, p. 246, and Cumulative Supplement, Key No. 359.

Marihuana or Hashish

Interest in hashish, also known as marihuana, as a factor in the production of insanity, crime, and drug addiction has been aroused during the last 10 years in the United States. Its common use is in the form of cigarettes. W. Bromberg considered that there were 2 categories of mental reaction, the first an acute intoxication or hashish psychosis, the other a toxic psychosis. The latter class was subdivided into (i) those cases showing a disturbed sensorium with delusions and emotional reactions, constituting a psychosis, but with the common characteristic toxic signs, and (ii) atypical functional psychoses either initiated or coloured by hashish. A third group, apparently not observed in American clinics, acquire chronic dementia and deterioration as a result of prolonged use. Fourteen cases of acute intoxication and 17 of toxic psychosis were studied. Symptoms of the acute type included an increase in motor activity, sensation of excitement, confusion, lightness of the extremities, swelling of the head, elementary visual illusions, disorientation, loss of perception of time, euphoria, and sexual disturbances. Subjective impressions of brilliance and clarity were common, but were actually translated into confused speech and memories. Uneasiness and frightening somatic illusions were frequently encountered when the drug was first smoked. In the second group, alcohol or other drugs may be involved, and as the toxic elements recede, the underlying functional psychosis develops and may last for weeks or months.

The personality of the patient was found to play a large part in this type; the use of hashish must only be considered as a factor, and not over-stressed. These patients frequently go on to heroin or morphine, finding that hashish is not strong enough to overcome the inadequacies of which they are conscious. Generally speaking, the use of this drug was not thought to predispose to crime, most of the convictions of addicts being for the sale and possession of the drug, which is contraband. Increase in dosage does not appear to be necessary, and the effects of withdrawal seem to be negligible. The question of habit formation is apparently a doubtful point, and appears to be regulated by the number of times the user wishes to experience the sensations produced by the drug.

Bromberg, W. (1939) *J. Amer. med. Ass.*, **112**, 4.

DRUG ERUPTIONS

See also Vol. IV, p. 261, and Cumulative Supplement, Key No. 360.

Sulphanilamide Rashes

Sulphanilamide therapy may result in several distinct types of toxic rashes, of which J. W. Tedder recognizes 3. The most common type is precipitated by exposure to sunlight, and is limited to the parts of the body exposed. The second type is that in which there occurs a definite sensitivity to the drug, resulting in a sensitization dermatitis, the patient being unable to tolerate any further sulphanilamide therapy. The third type results from poor toleration of, or saturation with sulphanilamide and presents the typical picture of dermatosis. The patient can tolerate further sulphanilamide therapy providing excretion again becomes normal and the dosage is properly modified.

A case report is presented by D. E. H. Cleveland describing an eruption which occurred in a native of India, presumably as a result of the administration of 600 grains of sulphanilamide by mouth in 9 days. The rash, which was not confined to exposed parts and did not cause itching, in some respects resembled erythema multiforme. The uniformly predominating pustular lesions justified the description of varioliform. After 2 weeks of bathing twice daily with a zinc and copper sulphate solution the rash cleared. There was no scarring.

Cleveland, D. E. H. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 693.

Tedder, J. W. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 217.

Mercurial Rash

E. F. Traub and R. H. Holmes reported 2 cases of mercurial poisoning, characterized by soreness of the mouth and skin eruptions, due to the presence of amalgam fillings in the teeth. The danger of chronic mercurial poisoning from this source, however, is very slight and it is believed that only hypersensitive persons are susceptible. Acute symptoms of poisoning may occur. The presence of mercury in the urine may be taken as a diagnostic sign, but only if it is in excess of the normal amounts.

Traub, E. F., and Holmes, R. H. (1938) *Arch. Derm. Syph., N.Y.*,

38, 349.

DWARFISM AND INFANTILISM

See also Vol. IV, p. 277.

Infantilism with Webbing and Cubitus Valgus

An extremely rare syndrome of infantilism, webbing of the skin of the neck, and deformity of the elbow (cubitus valgus) is reported by H. H. Turner in seven females between the ages of 15 and 23 years. Treatment with anterior-pituitary growth hormone was unsatisfactory, but definite genital development followed administration of the anterior gonadotrophic hormone in the two cases thus treated.

Turner, H. H. (1938) *Endocrinology*, **23**, 566.

DYSENTERY, BACILLARY

See also Vol. IV, p. 317, and Cumulative Supplement, Key No. 364.

Treatment*Pectin and Metal Pectinates*

Pectin and certain pectinates were studied by L. Arnold with regard to their bactericidal action. Pectin was found to have none, while the metal pectinates, particularly silver, possess definite bactericidal properties. Unlike pure pectin, the metal pectinates are soluble in water. The preparation is stable and non-toxic, the metal ion acting similarly to a colloidal compound attached to pectin as a vehicle. Further study should establish the clinical usefulness of these compounds in bacillary dysentery, in the treatment of burns of the skin, and in the post-operative treatment of osteomyelitis.

The results obtained by the use of pure pectin and nickel pectinate in acute and chronic bacillary dysentery are reviewed by L. H. Block *et al.* Twelve acutely ill patients were treated with pure pectin (granules), 6 tablespoonfuls a day being administered, but the results were entirely disappointing, no relief from symptoms being exhibited. Seven of the patients, however, showed an increase in weight. In contradistinction, the use of nickel pectinate provided striking improvement. Ninety-five patients were treated by administering two fluid ounces every three hours for 14 days, succeeded by an interval of 25 days, and followed by a further 21 days of treatment, 9 days of rest, and a final course of therapy lasting 12 days. In general, and with few exceptions, improvement occurred in the appearance and general condition of the patient during the treatment periods, but there was some decline during the interval. The temperature dropped, tenesmus and abdominal cramp disappeared, and increased appetite was noted. No bloody stools were found during this treatment, and there was an increase in weight. Twenty-nine patients recovered during the period of investigation. The author is convinced of the value of this therapy in bacillary dysentery.

Calcium and Kaolin

B. L. Greene and L. H. Block treated a series of 60 cases of acute bacillary dysentery with combined calcium and kaolin therapy, thereby reducing the mortality by over 50 per cent. The dosage advocated was the intravenous or intramuscular injection of 10 c.cm. of 20 per cent calcium glucono-galactogluconate twice daily, accompanied by 2 drachms each of kaolin and calcium gluconate with an equal amount of Cal-C-Malt given orally every two hours. The combined use of calcium and kaolin gives better results than treatment with either substance alone. This treatment is a valuable adjunct to other established medical measures. Parathyroid extract does not intensify the action of calcium.

Arnold, L. (1939) *Amer. J. digest. Dis.*, **6**, 104.

Block, L. H., Tarnowski, A., and Green, B. H. (1939) *Amer. J. digest. Dis.*, **6**, 96.

Greene, B. L., and Block, L. H. (1938) *Amer. J. digest. Dis.*, **5**, 684.

DYSIDROSIS

See also Vol. IV, p. 349.

Hidradenitis Suppurativa

H. A. Brunsting reviewed 22 cases of hidradenitis suppurativa, a chronic indolent inflammatory disease of the skin and subcutaneous tissue characterized by the formation of abscesses and sinuses and involving the axillary, mammary, inguinal, genital, and peri-anal regions, in which the apocrine type of sweat gland is present. Causation is obscure, but the presence of a traumatic factor as a sequel to contact dermatitis or irritation caused by application of deodorants or depilatories, or frequent shaving of the axillary hair, is suggested. The disease chiefly affects young adults; frequent relapses occur. Smears and cultures in a series of cases showed the haemolytic streptococcus, *Staphylococcus aureus*, *Staphylococcus albus*, and *Streptococcus viridans*, but it is considered that a fertile soil may play as important a part

as the presence of a specific bacterial organism. Treatment in the early stages includes prompt incision of the individual abscess with adequate drainage, and the use of filtered X-rays. Local therapy includes ultra-violet irradiation, zinc peroxide paste, and sulphur baths. The administration of sulphanilamide is of value when the disease is far advanced. Total excision with destruction of all the glands in the affected area, followed by plastic repair, may be necessary.

Brunsting, H. A. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 108.

DYSMENORRHOEA

See also Vol. IV, p. 353.

Aetiology

C. F. Fluhmann made 85 tests for oestrogenic substances on the blood of 19 patients with primary dysmenorrhoea. In one case the oestrogen concentration increased at the time of menstruation and there was no rise during the mid-interval; but all the other patients did not show any departure from the normal. These observations militate against the hypotheses that primary dysmenorrhoea is due to deficiency or excess of either oestrin or progesterone.

Fluhmann, C. F. (1938) *Endocrinology*, **23**, 393.

Treatment

Thyroid

R. C. Foster and M. J. Thornton treated 50 patients, between the ages of 16 and 31, with menstrual disorders with desiccated thyroid. All the patients had a basal metabolic rate below zero, the average being -15. Out of 25 patients with dysmenorrhoea, 17 obtained complete, 5 partial, and 3 no relief. Seventeen patients with oligomenorrhoea all obtained relief from this treatment. Only one out of the 4 with amenorrhoea was benefited; out of 13 with metrorrhagia, 12, and 6 out of 7 with menorrhagia, obtained complete relief.

Insulin

E. W. Schrick contended that malnutrition plays an important part in the aetiology of dysmenorrhoea. The treatment of this underlying factor with insulin, together with carbohydrate, was followed by improvement, and the author concluded that stimulation of the ovaries was the factor responsible for improvement.

Foster, R. C., and Thornton, M. J. (1939) *Endocrinology*, **24**, 383.

Schrick, E. W. (1939) *Amer. J. Obstet. Gynaec.*, **37**, 146.

DYSPEPSIA

See also Vol. IV, p. 367.

Differential Diagnosis

D. L. Wilbur and J. H. Mills investigated the accuracy of a diagnosis of functional dyspepsia in 354 patients and found that the original diagnosis proved correct in 94 per cent of cases over a period of 5 years. It was found that 11 per cent of a total of 39 patients similarly diagnosed within 5 years furnished evidence of organic disease of the gastro-intestinal tract, including duodenal and gastric ulcer, gall-bladder disease, and carcinoma. A group of 12 patients diagnosed originally as functional dyspepsia later showed various organic diseases outside the gastro-intestinal tract. In only 2 of these could a clear-cut relation be established between the original symptoms and the final condition. It seemed therefore that careful examination, particularly with the aid of the gastroscope, resulted in a considerable degree of accuracy attending a diagnosis of functional dyspepsia.

Wilbur, D. L., and Mills, J. H. (1938) *Ann. intern. Med.*, **12**, 821.

DYSпноEA

See also Vol. IV, p. 388.

Sighing Dysпноea

C. K. Maytum described the clinical syndrome associated with sighing dysпноea. Diagnosis may be based on the characteristic complaints of 'shortness of breath', 'being unable to draw a deep breath', a sensation of thoracic constriction and, frequently, palpitations. Such patients are usually highly nervous and over-anxious regarding their state of health. Fear and suspicion of organic disease are exciting causes. There is no wheezing or cough, but possible diagnoses such as asthma, coronary disease, or left ventricular failure should be excluded. Post-encephalitic hyperпноea resembles sighing dysпноea more closely than any other condition, but the breathing is more forced and noisy and the patient grimaces. Tetany, following sighing dysпноea, is sufficiently common to warrant the dysпноea being regarded as an aetiological factor in any case of tetany which subsequently develops. The physiological basis suggested as an explanation of sighing dysпноea is that limitation of respiratory excursion causes a slight oxygen deficiency which is relieved by deep breathing or by the administration of oxygen. Treatment consists of a rational explanation of his condition to the patient, attempts to relieve any nervous symptoms which may be present, and the administration of sedatives. If hyper-ventilation tetany is present, it may be controlled very quickly by the administration of carbon dioxide.

Maytum, C. K. (1938) *J. Allergy*, **10**, 50.

Dysпноea in Coal-Miners

J. N. Peterson *et al.* carried out full clinical investigation on 36 coal-miners whose respiratory disability compelled them to give up their occupation. Each man was observed carefully while he performed a measured piece of work on a bicycle ergometer. This observation, together with measurement of the minute volume of his expired air at rest and during and after the exercise, afforded a means of determining the degree of dysпноea. The patients were classified into 3 groups on the basis of radiological findings: (i) the 'cricket-ball' type, (ii) mottling and reticulation, and (iii) no radiographical evidence of gross lesion. The first group (10 in number) had vital capacities ranging from 1,758 to 850 c.cm., with an average of 1,263 c.cm. per square metre of body surface; group (ii) (with 15 members) containing the more dysпноic and severely incapacitated, varied from 1,599 c.cm. to 595 c.cm. with an average of 1,051 c.cm.; and group (iii) (comprising 11) 2,694 c.cm. to 1,013 c.cm. with an average of 1,667 c.cm. The vital capacity per unit of body surface provided a more reliable estimate of the degree of respiratory incapacity than radiographs.

Peterson, J. N., Peterson, J. M., and Startup, C. W. (1939) *Lancet*, **1**, 147.

EAR DISEASES

See also Vol. IV, p. 402, Cumulative Supplement, Key Nos. 374-384; and pp. 86 and 94 of this volume.

Neurological Conditions Associated with Ear Diseases *

S. L. Shapiro described the neurological conditions seen by an otologist and characterized by an abnormal accumulation of cerebrospinal fluid, and sometimes termed arachnoiditis. There are signs of increased intracranial pressure and the cerebrospinal fluid is either normal or shows a mild meningitic reaction, simple relief of the pressure giving a permanent cure. The condition is not uncommon and may be due to trauma, disease of a contiguous bone, generalized infections, such as scarlet fever and influenza, or diseases of the central nervous system, and, when occurring in the posterior or middle cranial fossa, predominantly to aural causes. The condition is divided into four morbid types, namely (i) the fibrous and adhesive; (ii) the cystic in which a pseudocyst is formed in the affected area as a result of the obstruction to the normal flow of cerebrospinal fluid usually caused by inflammation of one of the cisterns; (iii) internal hydrocephalus due to inflammatory closure of one or more of the foramina or hypersecretion and so-called mechanical

obstruction of the foramina; and (iv) generalized intracranial hypertension with free communication throughout the subarachnoid space. Shapiro also divided the cases into 3 clinical classes and gave examples of the first and second occurring after inflammation of the ears. They are (i) cases which suggest a brain tumour; (ii) cases in which brain abscess appears probable; and (iii) cases in which there is a relatively sudden rise of intracranial pressure with severe symptoms but without focal signs. The condition is difficult to diagnose and may only be suspected when it is cured spontaneously or after lumbar puncture. When suspected, exploration of the dura is indicated if there is not any improvement after a reasonable period.

Shapiro, S. L. (1938) *Arch. Otolaryng.*, Chicago, **28**, 546

Actinomycosis

Thirty-one cases of actinomycosis of the ear have been reported, 15 occurring in the middle ear. O. C. Risch reviewed the literature of these cases and reported one which occurred in a man of 42 in whom it was discovered at a second operation for lateral sinusitis and bone necrosis following a mastoidectomy. Actinomycosis may be a primary or secondary invader in the ear, and Risch suggested that it gains entrance to the middle ear, either by continuity or through the Eustachian tube

Risch, O. C. (1939) *Arch. Otolaryng.*, Chicago, **29**, 235.

Acute Otitis Media

Aetiology

Following dysentery.—J. Nevelson examined 183 dysenteric children whose ages ranged from a few weeks to 5 years. Of these, 56 cases, or 30.6 per cent, had middle-ear inflammation. The distribution was as follows: of 72 children under one year otitis was found in 37.5 per cent, of 72 children between 1 and 2 years in 34.7 per cent, of 25 children between 2 and 3 years, in 12 per cent, and in 14 children between 3 and 5 years in one case, i.e. 7.1 per cent. In 4 children otitis appeared within the first 4 days of dysentery, but in most cases it developed after the twelfth day. In all the cases of dysentery complicated with otitis, leucocytosis was found, there being an increased number of neutrophils. Usually both ears were affected. Many of the children with otitis were restless and excited, and any pressure on the skin caused shrieking. The early diagnosis of otitis in children suffering from dysentery, especially in cases in which there are other complications, is most difficult without examination of the ears.

Diagnosis

Sedimentation rate.—J. R. Hume and H. Kahn attempted to assess the significance of blood sedimentation in acute otitis and its complications. It was found that the sedimentation rate remained within normal limits in an uncomplicated acute otitis, but when the serous effusion became purulent the rate was raised. It was concluded that the sedimentation rate was related rather to the actual destruction of tissue, while the blood picture showed the presence of acute inflammatory processes. Should further investigations support this view, the authors suggest that it would become a valuable diagnostic aid in cases of mastoid and middle-ear disease in which progressive destruction might be at work. No definite relation between the sedimentation rate and the blood picture was apparent. An interesting point was observed in 3 of the 10 cases reviewed. Massive destruction of tissue and necrosis of bone were present, and after operation the sedimentation rate showed a sharp rise with a gradual return to normal. It was thought that this second rise was associated with further damage to tissues consequent upon surgical intervention.

Treatment

Sulphanilamide. Studies on the sulphanilamide treatment of 22 children with acute otitis media or acute mastoiditis, and of 2 children with meningitis and one with septicaemia of otitic origin, were made by D. C. Baker and G. E. Bradford. The ages of the children ranged from 4 months to 12 years with the exception of a 17-year-old boy. The dosage of the drug was based on body weight; an average of 0.1 g. per kg. of body weight was given daily, divided into 4 doses. The solution used contained 0.8 g. in 100 c.cm. of sterile physiological solution of sodium chloride. The authors found that sulphanilamide is of use in the treatment of acute otitis media and acute mastoiditis, and may prevent operation in the latter. It does not kill the streptococci in the bone. It is useful in the treatment of meningitis, and, in

the one case of bacteraemia in this series, although mastoiditis was present, the patient recovered without operation.

Baker, D. C., and Bradford, G. E. (1939) *Arch. Otolaryng.*, Chicago, **29**, 334.

Hume, J. R., and Kahn, H. (1939) *Arch. Otolaryng.*, Chicago, **29**, 820.

Nevelson, J. (1939) *Vrach. Dyelo*, **21**, 243.

Chronic Otitis Media

Clinical Picture

Cholesteatomas.—Cholesteatomas of all types are epithelial in origin. Many observers think that the epithelium is formed by metaplasia following infection, leading to the formation of squames and polyps. A. Tumarkin considers that the epithelium may occur in the mastoid bone as a congenital or early infantile phenomenon because cholesteatoma always occurs in certain types of mastoid bone, namely the poorly-pneumatized or the ivory type. Acute epitympanitis, which may be considered the forerunner of this condition, also occurs in these types of bone. Attempts to form a cholesteatoma by grafting skin into the mastoid sinus have failed. Removal of the cholesteatoma results in epithelialization of the cavity, and Tumarkin condemns the destruction of the surrounding bone on the assumption that it is sclerosed. Bondy's transmastoid atticotomy is considered a suitable operation in these conditions, and trans-meatal atticotomy is even better. In the treatment of chronic epitympanitis any polyp present must be destroyed or it will obstruct drainage. The author recommends that this condition should be treated by the comparatively simple operation of trans-meatal atticotomy, followed by mastoidectomy if necessary.

Treatment

Urea and caroid.—The application of urea, combined with caroid, as a new treatment for chronic otitis media is discussed by G. E. Tremble. He recommends a powder mixed in the proportion of 60 parts of urea powder, 15 parts *Carica Papaya* (caroid), and 25 parts of boric acid. This powder has valuable bactericidal and deodorizing properties. It is quite harmless to normal tissues on which it has a stimulating effect, and it has a definite action on necrotic tissues, dissolving pus and epithelial debris, and thus encouraging normal healing. The ear is dried thoroughly and a freshly prepared saturated solution of the powder is run into the meatus and left for a few minutes with the patient's head on his side. These drops are instilled night and morning. If the discharge becomes more profuse after a few days owing to liquefaction of the pus, a solution of urea and caroid in 25 per cent alcohol is very useful.

Tremble, G. E. (1939) *Canad. med. Ass. J.*, **40**, 149.

Tumarkin, A. (1938) *J. Laryng.*, **53**, 685.

Acute Mastoiditis

Treatment

Sulphanilamide.—Sulphanilamide as a routine treatment in every case of acute suppurative otitis media attending the Royal Naval Hospital, Chatham, was described by V. G. Horan and S. Gay French. The incidence of acute mastoiditis in acute otitis media had, since this procedure was begun, fallen from 22.7 to 4.5 per cent. Whereas the number of deaths annually from this complication formerly averaged 2.85 per cent, there had not been any death from this cause during the last year. Treatment lasted 14 days, and the following technique was employed. On admission all patients with acute suppurative otitis media were given colsulanyde (elixir sulphanilamide), 1 fluid drachm by mouth 4-hourly; a smart sulphur-free purge and a sulphur-free analgesic such as aspirin. The long-established local treatment of the disease was also carried out, namely: myringotomy, if the tympanic membrane showed signs of retained pus; whether perforation had or had not taken place, syringing the ear thrice daily with saline or a solution of boric acid, followed by drops, those mainly used being drops of dilute ointment of mercuric nitrate, of boric acid in alcohol, or of glycerin of phenol; and when the tympanic membrane was inflamed, intact, but not bulging, sedonan or otalgan; constant inhalations of

compound tincture of benzoin and menthol; and attention to nasopharyngeal and sinus infection.

Horan, V. G., and French, S. G. (1938) *Brit. med. J.*, **2**, 942.

Complications of Suppuration in the Middle Ear

Otogenic Meningitis

Treatment.—S. J. Kopetzky thinks that the removal of the bone focus is the first step in the treatment of otogenic meningitis. Every part of the temporal bone must be searched in order to locate the penultimate lesion. It is important to render the cerebrospinal fluid as nearly normal as possible, and whole blood transfusions have been found the most successful method of effecting this. They should be given in small amounts, repeatedly, at intervals of 1 or 2 days. Sulphanilamide, given in doses large enough to saturate the body fluids as rapidly as possible, has proved useful.

Kopetzky, S. J. (1938) *Amer. J. Surg.*, **42**, 131.

Operations on the Ear

Mastoidectomy

J. A. Sullivan described the technique of an operation, designed to obviate the risk of injury to the facial nerve in the mastoid operation, which he performed on 60 cases. (i) The tympanic segment of the nerve might be injured in the simple mastoid operation. The position of the horizontal canal is fixed, its anterior margin being constituted by the posterior border of the Fallopian aqueduct which must always be recognized when the mastoid antrum was opened, because it affords a protection to the nerve. (ii) In the radical operation the tympanic segment must be visualized by determining and recognizing the processus cochleariformis which shows the anatomical position of the nerve on the internal wall of the middle ear. The 'bridge' should never be removed by any manipulation directed from the middle ear towards the mastoid antrum. (iii) The nerve in sclerotic bone is more superficial on the tympanic aspect of the posterior bony canal wall, and is most prone to injury in the lowering of the hypotympanum and the removal of the bony margin of the annulus tympanicus on this surface. If attention is paid to these points, this complication would rarely arise, and would carry an improved prognosis.

Transmastoid Drainage

F. Tyrer Madge recorded the results of transmastoid drainage of the ear in 103 cases of chronic suppurative otitis media. This operation was performed on children with a history of suppurative otitis media of more than 6 weeks' duration without any response to conservative treatment. All cases of acute mastoiditis were in a separate category. The operation consists in the removal of the cortical cells of the mastoid process and opening the mastoid antrum to allow free drainage of the middle ear via the aditus through the post-auricular wound. The post-operative treatment was either to irrigate the middle ear with antiseptic lotions through the post-auricular wound or to continue the application of zinc ionization. The criterion of success was fixed as the production of a dry healed scar within 3 months of the operation. The cases treated were divided into 3 groups: (i) early cases, chronic suppurative otitis media of 6 to 12 weeks' duration; (ii) a group with a history of 3 to 6 months, (iii) a group with a history of more than 6 months. The percentage of successes was 51 in the first group, 38 in the second, and 40 in the third.

Lempert's Technique

In connexion with Lempert's technique for approaching the mastoid through the external auditory meatus, the so-called endaural approach, W. Howarth and G. H. Bateman point out that the triangular window made in the posterior superior meatal wall gives an excellent view of the mastoid antrum, and the extension of the initial incision forwards and upwards increases the possibility of mobilizing the soft tissues on the underlying bone. In 30 cases thus treated, 20 being acute mastoiditis and the remaining 10 chronic suppurative otitis media, packing was not required in the acute cases.

Howarth, W., and Bateman, G. H. (1938) *Lancet*, **2**, 1168.

Madge, F. T. (1938) *J. Laryng.*, **53**, 711.

Sullivan, J. A. (1938) *Canad. med. Ass. J.*, **39**, 451.

ECZEMA

See also Vol. IV, p. 447, Cumulative Supplement, Key No. 386; and p. 63 of this volume.

Clinical Picture

H. D. Niles described a condition which attacked the extensor surfaces of the arms, occasionally extending to the forearm and shoulders. Round, circumscribed, dry, red, scaly patches appeared, varying in size from a pea to a small coin, with the appearance of a fungous infection. Histological examination revealed no fungoid infection. Patch tests with possible external irritants yielded negative results. There was an accompanying pruritus. The condition occurred chiefly in young adults in those classes where daily or twice daily baths are customary, and most patients admitted careless drying of the arms after immersion. The eruption came on in the winter, and tended to disappear spontaneously in the summer. Treatment consisted of less frequent bathing, careful drying of the arms, the use of a superfatted soap, and the application of an ointment containing salicylic acid 10 grains, oil of eucalyptus 60 minims, bismuth subnitrate 60 grains, made up with wool fat and ammoniated mercury ointment to 1 ounce. The symptoms resolved in one or 2 weeks, but tended to return when the ointment was discontinued.

Niles, H. D. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 474.

ELECTROTHERAPY

See also Vol. IV, p. 490, and Cumulative Supplement, Key No. 389

Ionization

Aconitine Iontophoresis in Rheumatism

M. Barakin discussed the use of aconitine by ionization in rheumatism. He used a 1 per cent solution of the alkaloid and a current of 2.5 milliamperes. Iontophoresis was continued for 30 minutes. The active electrode was placed towards the periphery of the nervous network of the affected part. In the 6 cases described the results were remarkably stable and beneficial. This, in the author's view, was due to the local analgesic action of the drug, which also had a marked action on oedema which disappeared completely under iontophoresis; the circulation also improved, and parts formerly cyanotic became normal. In certain cases an antispasmodic action was observed. The author emphasized the inadequate number of clinical cases seen, and hoped to be able to make further trials with this method.

Barakin, M. (1939) *Ann. Méd. phys. Rhumat.*, **32**, 125.

Short-Wave Therapy

The Rotating Electrode

The clinical results obtained by the use of the rotating electrode, particularly in nasal conditions, has led J. P. P. Stock and C. R. Burch to advocate its substitution for the stationary electrode. The advantages are several. Treatment by this means is more pleasant; 'hot spots' on the skin and pricking sensations do not occur, improvement appears earlier, and sometimes a dramatic immediate result is obtained during treatment. Caution is necessary at first in order to ascertain the amount of reaction which may be produced, as it is felt that the rotating electrode is more potent than its stationary counterpart. Patients tend to stay in resonance longer without the necessity for re-tuning. The author maintains that better results are obtained in chronic inflammatory conditions by using greater current strengths in the patient circuit. The distribution of a 6-metre current is discussed, and 3 advantages of this type of short-wave therapy are found to be (i) that the capacitative impedance of the fat layers is not so great as to exclude 6 metres completely from the region that they surround; (ii) that at 6 metres appreciable heat can be developed in fat without the use of excessive voltages; and (iii) that the 6-metre current can conveniently be led into the patient through an air space. It is shown that the impedance of air or gas in a cavity in the body will be very much greater than that of an equal volume of tissue. Accordingly, nearly the whole current will flow outside gas

cavities, and the only way to heat the whole of the surface of a cavity is to change the direction of the line of flow of current periodically. The rotating electrode is particularly useful for facial treatments. A fairly small electrode is used, and moved so as to heat the various regions, thus obtaining a better approximation to a constant power supply. Further, the use of a rotating electrode allows smaller air gaps with diminished loss of power.

Stock, J. P. P., and Burch, C. R. (1938) *Brit. J. phys. Med.*, N.S. 1, 406.

EMPHYSEMA OF THE LUNGS

See also Vol. IV, p. 508.

Interstitial Emphysema

Evidence is brought forward by L. Hamman that interstitial emphysema, due to rupture of the pulmonary alveoli, may occur spontaneously without injury or unusual distension of the lungs, for example during mild walking, sitting in a chair, or resting on a bed. When the amount of escaped air is small, there may be thoracic pain only; when a larger leakage of air occurs, the air may pass into the pleural cavity and cause a spontaneous pneumothorax, or it may track into the mediastinum. In the latter event the symptoms may be severe and imitate coronary thrombosis or pericarditis. Hamman described a new and characteristic physical sign, namely a peculiar crunching, crackling, bubbling sound heard over the heart with each contraction. In addition the cardiac dullness may be diminished or its place taken by a tympanitic area, and radiology may show air in the mediastinum. The symptoms do not last long.

Hamman, L. (1937) *Trans. Ass. Amer. Phys.*, 52, 311

ENCEPHALITIS EPIDEMICA

See also Vol. IV, p. 546, and Cumulative Supplement, Key No. 399.

Post-Encephalitic Parkinsonism

Treatment

Bulgarian belladonna.—F. J. Neuwahl recorded the results of Bulgarian belladonna treatment of 123 patients with post-encephalitic Parkinsonism. He found that the large initial dosage recommended by Raef and employed by Hill might cause toxic symptoms sufficiently serious to lead the medical attendant or the patient to abandon the treatment; the mental effects, especially confusion, hallucinations, and delirium, contra-indicated the use of Bulgarian belladonna in general practice. For the preparation of the decoction in white wine a method of cold extraction was substituted. The activity of this solution did not deteriorate after a few weeks. The average alkaloidal content of the English root was slightly less than that of the Bulgarian, and in order to produce the same effect the dose of the English root must be 10 to 20 per cent higher. Patients with extremely serious forms of Parkinsonism, and probably still with a chronic infection which overcame the local cellular immunity, were not suitable for this treatment.

Treatment is commenced with 3 c.cm. of the extract, the doses being increased by 1 to 2 c.cm. every day, or every second day; by this gradual method a daily dose of 80 and even 120 c.cm. was reached without toxic signs except blurred vision and a dry mouth. The maintenance doses did not exceed 55 c.cm. daily, the lowest being 5 c.cm. daily. The more favourable results of the Bulgarian treatment might be due to 3 factors: (i) the natural distribution of the alkaloids in the root; (ii) the possible presence of buffer substances; and (iii) the synergism and different actions of the 3 alkaloids—scopolamine, hyoscyamine, and atropine—contained in the extract. The patient's toleration of the drug diminished, in proportion as a normal state of health was attained. The effects might become cumulative. The dosage must be decreased in hot weather. The extract acts as a great spur to most lethargic and irritable patients. Of the 123 patients treated, 2 died of intercurrent disease and 3 of a recurrent attack of encephalitis. Of the remaining 118 submitted to this treatment, 43 per cent showed a symptomatic cure, 23 per cent greatly improved, 25 per

cent revealed moderate improvement, and 2 per cent only slight improvement. Forty-seven per cent were able to resume work. The duration of treatment was up to 15 months.

Neuwahl, F. J. (1939) *Lancet*, 1, 693.

ENCEPHALO-MYELITIS

See also Vol IV, p. 553, and Cumulative Supplement, Key No. 400.

Acute Disseminated Encephalo-Myelitis complicating the Specific Fevers and Vaccination

After Vaccination

F. v. Herrenschrand described an affection of the optic nerve in cases of post-vaccinal encephalo-myelitis. Acute retrobulbar neuritis had been observed during life. The clinical signs were similar to those observed in cases of myelitis, disseminated sclerosis, and epidemic encephalitis. On microscopical examination of the optic nerve, however, a difference was observed. In the cases of post-vaccinal encephalitis a continuous border of glial cells surrounding the veins of the optic nerve produced a characteristic picture. Other alterations observed in the optic nerve were the same as those observed in the brain in cases of this affection.

After Measles

J. Ziskind and H. J. Shattenberg pointed out that 3 views were held regarding the cause of encephalitis occurring in the course of, or after, measles: (i) the encephalitis is due to the virus of measles; (ii) it is an allergic or anaphylactic phenomenon; and (iii) it is caused by an unknown virus, separate and distinct from that of measles. No cause has been definitely established.

A full report is given of a boy, aged 5, who had an attack of measles 6 months before his admission to hospital. Death occurred 10 weeks later. Necropsy was performed and the most prominent histological feature was the perivascular proliferation consisting chiefly of glial cells. Scattered cells of a haematogenous nature were found in the perivascular spaces, mainly lymphocytes but also plasma cells. There was perivascular demyelination with the presence of fat-containing glial cells and hyperplasia of the endothelium lining the blood vessels. The clinical picture is not constant. Diffuse cerebral involvement tends to be replaced by localized phenomena. The encephalitis may be accompanied by (a) hemiplegia and aphasia, (b) paraplegia, and (c) a cerebellar or spinal cord syndrome. The cerebrospinal fluid presents no uniform picture but the pressure may rise as high as 400 mm.

N. Malamud reported 2 cases of encephalitis following measles. The first was a mongolian idiot of 14 who developed a right hemiplegia during the prodromal period of measles, with some pyramidal signs also on the left. There was a gradual improvement, but residual signs persisted. The child died 5 years later from miliary tuberculosis. There was wide-spread perivenous and subependymal demyelination in the white matter of the cerebrum and cerebellum, and marginal gliosis of the spinal cord, in addition to acute tuberculous meningo-encephalitis. The second case was a boy of 8 who developed coma on the fourth day of an attack of measles. There were typical signs of meningitis. The child made a good recovery, but was left in a state of euphoria and restlessness, with increased salivation, involuntary movements of the limbs, and impairment of both memory and concentration. The condition appeared to be a post-encephalitic hyperkinetic state. Death occurred 4 years later from an unknown cause. The pathological findings were similar to those in the first case.

Post-measles encephalo-myelitis differs both clinically and pathologically from the primary demyelinating disorders, such as disseminated sclerosis. In the first, the symptoms are transient or stationary, whereas in the second they are always progressive. Pathologically, post-measles encephalo-myelitis shows demyelination only in the areas above mentioned, and there is always evidence of acute inflammatory change.

Herrenschrand, F. v. (1939) *Klin. Mbl. Augenheilk.*, 102, 815.

Malamud, N. (1939) *Arch. Neurol. Psychiat.*, Chicago, 41, 943.

Ziskind, J., and Shattenberg, H. J. (1939) *Arch. Path.*, 27, 128.

Spontaneous Encephalo-Myelitis

In a report on the 1933 epidemic of encephalitis in St. Louis, T. C. Hempelmann stated that a filtrable virus was obtained which produced the disease in mice and monkeys and was neutralized by serum from patients recovering from the disease then epidemic, but not by the serum of individuals who had had epidemic encephalitis. The mode of transmission appeared to have been by contact infection rather than by means of food, water, or insects. Multiple cases in one family were very unusual. The cases were divided into three groups, although one type often merged into another: in type I the encephalitic symptoms predominated from the onset which was sudden with malaise, occasionally convulsions, rapidly followed by headache, vomiting, and high fever (103° to 105° F.). Stiffness of the neck and even of the lower spine was common, but not invariable. Other symptoms were muscular cramps, sore throat, photophobia, mental confusion, and increasing drowsiness. Kernig's sign was often positive and absence of abdominal reflexes was the rule in adults. The knee-jerks and plantar responses were irregular. Improvement usually coincided with the fall in temperature. In type II the symptoms were preceded by a definite period of invasion of from 1 to 4 days, and occasionally longer. Type III included the mild or abortive forms of the disease and was liable to be overlooked. The cerebrospinal fluid in all types was moderately increased in amount and pressure during the acute stages. The cell count was increased to between 50 and 300, the mononuclears always predominating.

The globulin was moderately increased and the sugar content at, or a little above, normal. There was usually a slight leucocytosis, but occasionally a well-marked leucopenia. The Schilling haemogram generally showed a slight shift to the left. Complications were more common in adults than in children and increased with the age of the patients. The most frequent immediate cause of death apart from the toxæmia was broncho-pneumonia or lobar pneumonia. There is at present no specific treatment for acute epidemic encephalitis. Lumbar puncture often afforded lasting relief from the headache, but further treatment must be entirely symptomatic, particularly the prevention of dehydration by cutaneous administration of Hartmann's or Ringer's solution and intravenous dextrose or sucrose.

Hempelmann, T. C (1938) *J. Pediat*, **13**, 724.

ENDOMETRIOSIS AND ADENOMYOMA

See also Vol. IV, p. 561, and Cumulative Supplement, Key No. 401.

Clinical Aspects*Endometriosis of Ovary*

C. R. Tuthill reported a case of malignant endometrioma forming a large cyst of the right ovary in a girl aged 19 years and with a male distribution of hair, which imitated an arrhenoblastoma.

Endometriosis of the Arm

E. Navratil described what was possibly the first observed and reported case of endometriosis in the muscles of the forearm. The patient, who at the time of the discovery was 25 years old, complained of a painful swelling in the muscular portion of the extensor carpi radialis muscle. At operation this revealed itself as a fibrotic nodule the size of a cherry, which was found on histological examination to be a typical endometriosis with chronic inflammatory reaction. The patient was consequently kept under close observation and, at a total extirpation of the internal genital organs and appendicectomy many years later, it was found that there was a coexistent adenomyosis of the uterus. The author concludes by drawing attention to the practical certainty of a metastatic origin by the blood stream.

Endometriosis of the Umbilicus

W. Berman reported a case of endometriosis of the umbilicus in a 40-year-old woman who complained of abdominal pain and pain in the umbilicus before, during, and after the menstrual periods. This condition appeared when the patient started menstruating, and had persisted ever since. The umbilicus was discoloured with a bluish tinge at menstruation, and the patient complained of extreme tenderness over it. Operative removal followed by section proved the correctness of the clinical

diagnosis (pelvic endometriosis and endometriosis of the umbilicus), and, after operation, the patient remained free of symptoms.

Berman, W. (1939) *Amer. J. Obstet. Gynaec.*, **37**, 503.

Navratil, F. (1939) *Klin. Wschr.*, **18**, 905.

Tuthill, C. R. (1938) *Arch. Surg., Chicago*, **37**, 554

ENDOMETRITIS, CERVICITIS, AND METRITIS

See also Vol IV, p 574.

Cervicitis

Treatment

A Jacoby compared the results obtained in the treatment of 150 cases of cervical inflammation by cauterization, coagulation, and conization, i.e. removal of cervical mucosa. The average time necessary to cure patients by cauterization was 4 months, by coagulation 7 months, and by conization 7.3 months. Repetition of the same method or application of another was necessary in one case originally cauterized, in 6 originally coagulated, and in 5 coned. Stenosis of the cervical canal followed coagulation, and more cysts appeared in about one-third of those patients coned. All three methods were satisfactory, but cauterization cured more quickly and with fewer complications than the other two. It was the method of choice in Nabothian cysts, cervical erosions, and chronic cervical inflammation.

Jacoby, A. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 656

ENDOSCOPY OF THE URINARY TRACT

See also Vol V, p 20

Cystoscopy

Technique

Anaesthesia M Chevassu reported on the use of self-administered nitrous oxide for urological explorations. Cystoscopy and catheterization are uncomfortable, if not painful, to the patient, and it has long been realized that the introduction of a safe and simple method of analgesia was needed to make explorations a complete success. By using a small nose-piece, applicable by the patient himself, the surgeon directs the patient to take a few deep inspirations, and the patient controls the quantity which he requires to inhale in order to escape pain and spasm in the region of the exploration. The author recommends this method for further trial, emphasizing its simplicity.

Chevassu, M. (1939) *Bull. Acad. Méd. Paris*, **121**, 878.

ENTERIC FEVERS

See also Vol. V, p. 50

Treatment

Sulphonamides

E. H. R. Harries *et al* treated 6 cases of enteric with prontosil and M & B 693, and a seventh case with a combination of M & B 693 and Felix's Vi-serum. All the patients recovered. Owing to the leucopenia commonly present in enteric, and the fear of causing agranulocytosis, the drugs were given in small doses. The sulphonamide drugs had a bacteriostatic effect on the bacteria in the blood stream, and therefore lessened the toxæmia. The most dramatic recovery occurred in a patient who received one injection of serum in addition to M & B 693. The duration of the illness and of convalescence was markedly lessened.

Harries, E. H. R., Swyer, R., and Thompson, N. (1939) *Lancet*, **1**, 1321.

EPILEPSY

See also Vol. V, p. 96, Cumulative Supplement, Key Nos. 424-432; and p. 124 of this volume.

Aetiology*Physiological Disturbance*

N. G. Propper considers that a specific stimulus is not needed for the production of an epileptic fit. An epileptic discharge may arise from any excitation, exogenous or endogenous, affecting any part of the nervous system. Such a discharge falls with a maximum of energy on nerve-cells. A substance able to cause cell excitation may be produced in any part of the nervous system; it does not remain at the site of its formation, but, by humoral current, may be transported into every part of the brain, so that a general convulsion results. It is also brought in touch with the endings of autonomic nerves in blood vessels. By convulsions and vascular alteration, histopathological changes occur in the brain, in the first place in the ganglion cells of the third layer and in the Purkinje cells of the cerebellum. With repeated fits these alterations become more and more intense. The first fit produces an alteration in nervous tissue such that, later on, a stimulus harmless to a normal brain will produce a fit.

Convulsant Toxins

Muck and Baumann produced an epileptic seizure in patients suffering from genuine epilepsy by spraying ethyl chloride on the radial artery. V. Pagnan confirmed this observation. Injection of 1 c.cm. of a 1 per cent solution of adrenaline produced no fit in such a patient. Contrary to an opinion maintained by other authors, Pagnan denied that a fit produced by injecting cardiazol in large doses was the same as a true epileptic fit. Pagnan gave an intramuscular injection of cardiazol (1 to 3 c.cm.) to epileptics in order to produce predisposition for epileptic fits; immediately after that injection he sprayed ethyl chloride for 40 to 50 seconds on the radial artery of the patient who was in a sitting position. A fit came on in 19 patients 5 to 10 minutes later; a negative result was observed in 25 patients.

Heredity

Heredity is not of great importance in epilepsy. Three different causes were established for epilepsy by O. Marburg: (i) an injury to the brain, (ii) a toxic cause either exogenous, like alcohol, or endogenous, for example disturbed endocrine glands, and (iii) a cryptogenic form in which a cause could not be demonstrated. A scar in the brain, and hydrocephalus were demonstrated in many cases of epilepsy. Surgical therapy, if possible, must be used. X-rays were useful very often, especially in the early stage. Vasospasm, which was formerly supposed to be the cause of an epileptic fit, definitely was demonstrated to be of no importance. Antispasmodic therapy gave no valuable results. Frisch observed increase of serum albumin before a fit, and increase of serum globulin after one. This observation may provide a clue to therapy; definite results, however, were not observed. Increased tissue fluid as well as increased permeability of cell membranes were demonstrated during an attack, and often also damaged cells near the tuber cinereum. This observation is of much interest as important centres of metabolism are situated near this part of the brain. In order to increase excretion of water, magnesium gluconate was given to epileptics. The best result was observed when magnesium was given in combination with barbituric acid. A third of the cases were improved by this treatment; in the remaining cases no improvement at all was observed.

Water Retention

Water, given in large quantities, will induce fits in many epileptics. I. Ziskind *et al.* requested 25 fasting patients to drink tap water at a uniform rate of 1,000 c.cm. each half-hour until 7,000 c.cm. had been drunk. The group consisted of 16 epileptics and 9 'normals' who were actually psychoneurotics. Convulsions supervened in 50 per cent of the epileptics tested, and in none of the controls. The authors found that blood dilution and water retention were greater in epileptics than in non-epileptics after excessive water intake. The authors suggested that this may be due to increased cell permeability in epileptics. Moderate or small amounts of water did not induce fits. Among the epileptic subjects those having fits after

taking large quantities of water showed greater blood dilution and water retention than the non-convulsive group. The authors were doubtful as to the efficacy of dehydration in controlling fits, because, whether the epileptic has a fluid intake of one or two quarts daily, there is no difference in the incidence of the fits.

Marburg, O. (1938) *Schweiz. Arch. Neurol. Psychiat.*, **42**, 323.

Pagnan, V. (1939) *Arch. Psychiat. Nervenkr.*, **109**, 182.

Propper, N. G. (1938) *Rev. neurol.*, **70**, 332.

Ziskind, E., Somerfeld-Ziskind, E., and Bolton, R. (1939) *J. nerv. ment. Dis.*, **89**, 52.

Time Relationship of Attacks

G. M. Griffiths and J. T. Fox discussed the forms of rhythm in the records of the fits of a large group of epileptics. Charts were made of the fits of 110 boys and men and of 4 women at epileptic colonies, showing the time of occurrence and type of every fit for a considerable period, in some cases as long as 10 years. The most easily understood rhythm is the monthly or menstrual rhythm in which fits spread over the week following the onset of menstruation. There can be an equally regular monthly incidence in men. Weekly rhythm was not observed. As regards time of the day, by far the highest incidence is between 6 and 7 a.m., there being a steady rise from 3 a.m. to this peak and a very abrupt fall from 8 a.m. The next most common time for fits is between 10 p.m. and midnight. The lowest incidences are between 5 and 9 p.m. and between 9 and 11 a.m. Patients whose fits occurred within an hour of waking in the morning, 'rising fitters', were particularly intelligent, and most of those whose fits usually occurred in the afternoon were low-grade or deteriorating cases. Phenobarbitone often tends to clear the period immediately following its administration, or pushes a peak further away from that time. Bromides do not often affect the time incidence but, when they do, they appear to have their greatest effect during the second 12 hours after their administration.

Griffiths, G. M., and Fox, J. T. (1938) *Lancet*, **2**, 409.

Diagnosis

Use of Cardiazol

H. Nachtsheim discussed the question as to whether the artificial production of convulsions with cardiazol had any diagnostic value, and whether the hereditary epileptic was more susceptible to cardiazol than any other type of epileptic or the non-epileptic. It had been found that small doses of cardiazol, insufficient to cause convulsions in non-epileptics, caused convulsions in genuine or hereditary epilepsy. Nachtsheim bred a strain of epileptic rabbits, the so-called white Viennese rabbits, for his experiments. Young rabbits had more convulsions than old ones. He found that, after injection of 0.08 c.c.m. of a 10 per cent solution of cardiazol per kg. of body weight, only 3 per cent of the old non-epileptic animals had convulsions; the figure for the old epileptic animals was 83 per cent; of the animals from the epileptic race but without spontaneous convulsions 40 per cent were susceptible. In young animals (3 to 9 months) the following percentages showed convulsions after injection of the above dose of cardiazol: non-epileptic race, 29 per cent; epileptic race without spontaneous convulsions, 61 per cent; epileptic animals, 76 per cent. The results showed that 17 per cent of the old and 23 per cent of the young epileptics did not react to the dose of cardiazol. The author concludes that epileptics are more susceptible to a minimal dose of cardiazol, and that production of the convulsions by cardiazol provides no diagnostic assistance in hereditary epilepsy.

Nachtsheim, H. (1939) *Dtsch. med. Wschr.*, **65**, 168.

Treatment

Phenobarbitone and Belladonna

Thirty-two patients with idiopathic epilepsy were treated for 6 months by A. E. Loscalzo with phenobarbitone $\frac{1}{4}$ to $\frac{1}{2}$ grain 3 times a day; most of them also received a mixture of potassium bromide $7\frac{1}{2}$ gr. and chloral hydrate $7\frac{1}{2}$ gr. 3 times a day. The number of fits was reduced to approximately 25 per patient during that time, but all the patients complained of lassitude, and some of drowsiness. Loscalzo then prescribed for 6 months tablets containing $\frac{1}{4}$ gr. of phenobarbitone and $\frac{1}{16}$ gr. of laevo-rotatory belladonna alkaloids. Half a tablet was given 3 times daily, or 4

times if the fits were more severe. The number of fits per patient was reduced to approximately 19, and in very few cases was there any complaint of lethargy or somnolence. In 40 per cent of cases there was also a decrease in the severity of the convulsions. Loscalzo believed that the therapeutic action of phenobarbitone was strengthened by the presence of belladonna.

Cardiazol

As fits result from injection of cardiazol in cases of schizophrenia, A. Erb and J. Posniak tested the use of this treatment in epilepsy. For the first intravenous injection 0.4 to 0.5 g. of cardiazol was given. Two injections were given every week. As the sensitivity for production of a fit by injection of cardiazol was diminished in most epileptics, the dose of cardiazol was progressively increased, so that, at the end of a treatment, 2 to 3 g. of cardiazol were given at a single injection. Usually an increase of 0.05 to 0.1 g. of cardiazol at every injection was necessary for the production of a fit. In some cases, however, the threshold stimulus increased more slowly. Spontaneous fits stopped during the period of injections as well as after the treatment was finished in all those cases of epilepsy in which repeated injections of cardiazol raised the threshold for fits. Among 19 cases of epilepsy which were treated by this method, fits ceased in 15. The longest remission observed up to the time of publication lasted 3 months; the final result of this treatment is therefore at present unknown.

Brilliant Vital Red

R. Osgood and L. J. Robinson injected intravenously brilliant vital red in a group of epileptics. They found that the number and severity of the convulsions were diminished in a little over half of the cases. In several there was an increase in the number of seizures. The drug tended to have a greater anticonvulsant effect in *petit mal* than in *grand mal* seizures. In no case was any permanent kidney damage encountered, but some patients showed 'renal instability'.

Erb, A., and Posniak, J. (1939) *Z. ges. Neurol. Psychiat.*, **166**, 581.

Loscalzo, A. E. (1938) *J. nerv. ment. Dis.*, **88**, 500.

Osgood, R., and Robinson, L. J. (1938) *Arch. Neurol. Psychiat.*, Chicago, **40**, 1178.

Focal Epilepsy

Treatment

Surgical—In the treatment of focal epilepsy and athetosis L. T. Furlow carried out a subpial resection of an area of cortex which, when stimulated with a unipolar galvanic electrode, reproduced the focal convulsive movements or sensory seizures. In the operation under local anaesthesia, the incised pia was gently rolled back to the edges of the sulcus and with a brain spoon the necessary amount of convolution was removed, care being taken to keep inside the pia. There was no bleeding, and the area originally outlined was removed with exactness. This removal must include all areas which, when stimulated, produce the movement or sensation sought. Out of 16 cases so treated, 7 had been completely relieved of attacks and 6 showed very definite improvement. There were 2 deaths, giving a group mortality of 12.5 per cent.

Furlow, L. T. (1938) *J. Amer. med. Ass.*, **111**, 2092.

Myoclonus Epilepsy

Myoclonus epilepsy may be (i) intermittent; (ii) the partially continuous myoclonia of Kojewnikow, or (iii) the progressive familial myoclonia of Unverricht. R. R. Grinker *et al.* describe 2 cases occurring in an epileptic and mentally abnormal family. In both cases the disease began with convulsions followed by myoclonia, intellectual deterioration, and cerebellar symptoms. Electroencephalograms in this condition showed fast waves, the opposite of *petit mal* when the waves are 5 times as slow. Barbiturates were found effective in abolishing myoclonic waves and twitches from the electroencephalogram.

Grinker, R. R., Scrota, H., and Stein, S. I. (1938) *Arch. Neurol. Psychiat.*, Chicago, **40**, 968.

EPIPHYSES, DISEASES AND INJURIES

See also Vol. V, p. 127.

Chondro-Epiphysitis*Aetiology*

R. L. Schaefer *et al.* investigated the osseous condition of 258 endocrinopathic patients between the ages of 8 and 15, and found that 35 per cent of them were suffering from chondro-epiphysitis. Of these nearly all showed evidence of primary or secondary hypothyroidism. In a control group of 99 patients showing no endocrine disturbance, only 7 per cent showed any involvement of the chondro-epiphysial structures. The authors therefore concluded that chondro-epiphysitis is of endocrine origin, is always due to hypothyroidism, and that its presence is pathognomonic of that condition.

Schaefer, R. L., Strickroot, F. L., and Purcell, F. H. (1939) *J. Amer. med. Ass.*, **112**, 1917.

EPISTAXIS

See also Vol. V, p. 142, and Cumulative Supplement, Key No. 439.

Aetiology*Spontaneous Haemorrhage into Maxillary Sinus*

S. S. Hall and H. V. Thomas report 12 cases of spontaneous haemorrhage into the maxillary sinus, a condition usually recognized only by methodical examination of the sinus in the presence of epistaxis. The haemorrhage was invariably unilateral, and every patient had existing or pre-existing hyperplastic maxillary sinusitis. No abnormality in the general condition, such as haemophilia or arterial hypertension, which could account for the haemorrhage, could be found. In no case was there a history of trauma. The haemorrhage was severe, in one case reducing the haemoglobin to 58 per cent. It was accompanied by burning pain in the inner canthal region of the same side and a sensation of tickling and itching high up in the nose. Two cases responded to treatment by antral lavage, but the remainder required a Caldwell-Luc operation to clear the antrum and arrest the haemorrhage.

Hall, S. S., and Thomas, H. V. (1938) *Arch. Otolaryng., Chicago*, **28**, 371.

ERUPTIONS, ANOMALOUS AND ATYPICAL

See also Vol. V, p. 146, and Cumulative Supplement, Key No. 440.

Achromia Flava Amycetica

A. Castellani described a case of achromia flava amycetica, which occurs in tropical and sub-tropical countries, chiefly in Central America and the West Indies. It is not regarded as of fungous origin but as possibly tropho-neurotic. It is characterized by non-tender, non-pruriginous, painless spots, usually on the face and neck which, when fully developed, have a smooth surface and, in negroes, are yellow. They do not proceed to complete depigmentation and occasionally become pigmented again. The disease must be diagnosed from tinea aspergillacea, leucoderma, yellow achromia, pinta, sunlight achromia guttata, naevus anaemicus, and Sabouraud's pityriasis alba. Treatment has not much influence; arsenic may be given internally and the spots painted with permanganate solution 1 in 500 to 1 in 100 in order to darken them. Preparations containing oil of bergamot may be applied, followed by exposure to the sun or to artificial ultra-violet light.

Castellani, A. (1938) *J. trop. Med. (Hyg.)*, **41**, 309.

Urticate Lesions*Aetiology*

J. G. Hopkins *et al.* investigated the phenomena associated with urticaria resulting from heat, cold, and psychic influence. Their experiments with heat indicated that

the urticaria was produced by a nerve impulse reaching the skin from some central heat-regulating centre, which had been stimulated by warmed blood from the heated extremity. The sympathetic nerves supplying the sweat glands have been said to be cholinergic, i.e. they stimulate the secreting cells by the release of acetylcholine at their terminals. The autonomic vasodilator fibres accompany the sensory nerves to the skin, supply the cutaneous vessels, and the liberation of acetylcholine at their terminations may be excited either by an increase in body temperature or by a purely psychic stimulus, such as fear or anger. To this generalized type of urticaria provoked by heat the name 'cholinogenic urticaria' has been applied. In the localized type induced by heat, the wheals result from the direct action of heat on the skin. Hopkins and his co-workers reported 16 female patients, from 12 to 43 years of age, whose sensitivity to cold induced attacks of localized urticaria, the wheals being localized to the part exposed to cold.

Hopkins, J. G., Kesten, B. M., and Hazell, O. G. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 679.

ERYSIPELAS

See also Vol. V, p. 154.

Treatment

Sulphonamide Drugs

W. R. Snodgrass *et al.* contrasted the antistreptococcal activities in erysipelas of: (i) sulphamido-chrysoidine (prontosil red), (ii) sulphanilamide (streptocide); and (iii) benzylsulphanilamide (proseptasine). There was little difference between the efficacy of (i) and (ii) when doses of 2 g. of sulphamido-chrysoidine (i) and 1 g. of sulphanilamide (ii) were employed. The method of administration to an adult should be (i) sulphamido-chrysoidine, 1.5 g. every 4 hours—i.e. 9 g. per day—until cure is established; thereafter 1 g. 3 times daily, for a further 14 days. (ii) Sulphanilamide: 1 g. every 4 hours—i.e. 6 g. a day—until cure is established, thereafter 1 g. 3 times daily for a further period of 14 days. The proseptasine (benzylsulphanilamide) was less effective in checking the spread of the lesion within the first 24 hours, and much less certain in eliminating toxæmia by the third day. The complication of temporary cyanosis was present in 30 per cent of all cases.

J. Nelson *et al.* furnish additional information concerning the efficacy of sulphanilamide in erysipelas by a report of 344 cases comprising 31 children under 12, 219 men, and 94 women. In adult cases the doses for first, second, third, and fourth days were respectively 100, 80, 60, and 40 gr. of prontosil (sulphanilamide) orally in divided doses. Children under 2 years received 2 or 3 tablets of 5 gr. daily, usually crushed and given with food or drink, 2 to 5 years 2 tablets of 5 gr. 3 times a day; 6 to 12 years 3 tablets of 5 gr. 3 times a day. The average number of days required for the pyrexia to resolve was 4, and the average duration of residence in hospital was 7 days. The mortality was 12.9 per cent among the children, and 1.5 per cent among the adults.

Nelson, J., Rinzler, H., and Kelsey, M. P. (1939) *J. Amer. med. Ass.*, **112**, 1044.

Snodgrass, W. R., Anderson, T., and Rennie, J. L. (1938) *Brit. med. J.*, **2**, 399.

ERYTHEMA

See also Vol. V, p. 159, and Cumulative Supplement, Key No. 442.

Erythema Nodosum

Ætiology

Six cases of erythema nodosum associated with acute tuberculosis of cervical lymph nodes are described by B. C. Thompson. In 3 cases the upper deep cervical (tonsillar) group of lymph nodes was involved; in 2 cases the supraclavicular group, and in one case the submaxillary followed by the submental and tonsillar groups of the same side. In 3 cases, the tuberculous infection is believed to have been recent, and to have gained entrance by way of the tonsil, septic follicular tonsillitis having been a contributory cause of this portal of entry, and possibly also of the subsequent

softening and suppuration of the tuberculous lymphadenitis. In the other 3 cases tuberculosis had been present for a number of years. The onset of erythema nodosum was accompanied by an exacerbation in the cervical lymph nodes. Phlyctenular kerato-conjunctivitis was present in 2 cases. As this is generally agreed to be tuberculous in origin, the identity of the cutaneous lesions as haematogenous tuberculous foci is suggested. The associated conditions of skin and eye underwent exacerbation and remission more or less coincidentally. On the other hand, in 3 cases in which the initial symptom was enlargement of the lymph nodes, this was observed to regress immediately following the appearance of erythema nodosum.

Erythema Nodosum

J. Suranyi described an unusual case in which erythema nodosum appeared to be the result of an allergy developing after severe attacks of tonsillitis. The child, aged 6, had a marked lymphatic diathesis, and lymph nodes were readily palpable in the inframandibular and cervical regions. No other signs were present, and tuberculosis was excluded by radiological and laboratory investigations.

Suranyi, J. (1939) *Arch. Pediat.*, **56**, 1.

Thompson, B. C. (1939) *Brit. med. J.*, **1**, 159.

ERYTHRAEMIA

See also Vol. V, p. 176.

Aetiology

High Altitudes

In an elaborate paper P. H. Symons of the Department of Physiology, University of Witwatersrand, Johannesburg, recorded the results of a carefully controlled investigation on the erythrocyte, haemoglobin, and iron content of the blood in normal subjects at the altitude of the Witwatersrand (6,000 feet). The subjects of the research were healthy adult laboratory workers and medical students, acclimatized by a minimum residence of several months at that altitude. Much attention was paid to various available methods of estimating the blood constituents, and it was urged that, before results are reported, the value of the standard for that method should be checked by duplicate analyses, using such absolute methods as spectrophotometry, oxygen or iron content. The results are arranged in tables occupying 4 pages, and give information about the values in males and females at various ages. The following conclusions were reached. There is an increase of the red blood-cells on the Witwatersrand, and this is due to the effect of altitude, the haemoglobin content is not significantly altered, the colour index is significantly decreased; the red blood-cells do not show any marked tendency towards microcytosis, and are apparently normocytic and slightly hypochromic; the mean erythrocyte count of normal adult females at an altitude of 6,000 feet is approximately 0.6 million less than that of normal adult males at the same altitude.

Symons, P. H. (1939) *S. Afr. J. med. Sci.*, **4**, 18.

Complication

Stem-Cellled Sarcoma

D. Perla and S. B. Biller recorded the case of a woman aged 47 who, when 30, had erythraemia with a red count of 11 millions; after treatment for 13 years by X-rays and benzene, she became progressively and severely anaemic; 6 months before admission to hospital a swelling appeared in the region of the right scapula, but almost disappeared under X-rays; the blood count then showed 3 million red cells, 14 per cent myeloblasts, and 6 per cent normoblasts. Tumours then appeared widely over the body, a large one over the sternum. The liver was enlarged. The urine did not contain Bence Jones' protein. Microscopically the sternal tumour was a haemopoietic sarcoma (primitive red-cell type) composed of primitive haemopoietic elements, chiefly haemocytoblasts, many erythroblasts, and normoblasts, arranged in a pattern similar to that in the red bone marrow. It was regarded as a stem-cell sarcoma of a primitive type, and due to over-compensation after exhaustion due to erythraemia.

Perla, D., and Biller, S. B. (1939) *Arch. Path.*, **27**, 902.

ERYTHROMELALGIA

See also Vol. V, p. 178.

Treatment*Acetylsalicylic Acid and Adrenaline*

L. A. Smith and E. V. Allen suggest that, in erythromelalgia of the extremities, relief lasting several days may be obtained by acetylsalicylic acid (aspirin) in amounts as small as 10 gr. and the injection or inhalation of adrenaline. More severe measures include section, crushing, or injection of alcohol into the posterior tibial or peroneal nerve, and an attempt to desensitize the skin to warmth.

Smith, L. A., and Allen, E. V. (1938) *Amer. Heart J.*, **16**, 175.

EYE EXAMINATION

See also Vol. V, p. 216.

Aniseikonia

With a view to ascertaining the clinical value of correcting aniseikonia, C. Berens and M. Loutfallah examined 836 patients, 711 in hospital and 125 privately. In the first of these two groups 132 had no aniseikonia, and in the second 31 were found to be negative. Of the remaining patients 368 in the hospital group and 50 in the private group received isekonic lenses. Improvement was noted in 73 per cent of the 368 hospital patients, and in 74 per cent of the 50 private patients.

Certain circumstances control the testing for aniseikonia by the ophthalmokinometer, the instrument used by the authors. Patients are tested successively for binocular single vision, visual acuity, heterophoria, astigmatism, and aniseikonia. The patient must possess sufficient vision to be able to observe spots and lights on the screen, and must also have simultaneous binocular perception. There must be no defect in the central field, and there must be ability to fuse the images of the large central fixation spot. Aniseikonia was not considered to be an independent condition, but was found to occur in conjunction with heterotropia, ametropia, anisometropia, and with reading difficulties.

The clinical picture includes visual disturbances such as blurred vision, diplopia, fixation difficulty, squint, and photophobia, with symptoms which may be referred to the gastro-intestinal or nervous systems. It was considered that the underlying cause of this condition might be optical, anatomical, or possibly neuropsychological. Two types were predominant: the first was an overall difference in which one image was larger than the other in all meridians; the second was a meridional difference in which there was an inequality of images in one meridian. Herzau and Ogle apparently held that correction of aniseikonia was of little importance, because the compensating mechanism, acting in asymmetrical convergence, might also be effective with the eyes in the primary condition. The authors concluded, however, from their results that considerable improvement occurred from the correction of aniseikonia, and that, when visual disturbances, ocular fatigue, and vertigo were not relieved by ordinary correction, examination for aniseikonia should be performed and isekonic lenses supplied if necessary.

Berens, C., and Loutfallah, M. (1939) *Amer. J. Ophthalm.*, **22**, 625.

Use of Paredrine

The actions of atropine and benzedrine on the eye are discussed by I. S. Tassman, and it is shown that the synergistic effect of these two drugs is explained by the fact that atropine acts as a synergist of any adrenergic drug by removing the acetylcholine action as a brake or check on the adrenergic activity. Myerson and Thau had suggested that this synergism might be useful in producing complete cycloplegia of short duration.

Paredrine is closely related to benzedrine and has the same effect on ocular accommodation, but is less irritating, and has no demonstrable effect on the intra-ocular tension.

Investigations were undertaken by the author as to accommodation, the size of the pupil, and the length of cycloplegia. After the instillation of one drop of a 1

per cent aqueous solution of paredrine hydrobromide there was a dilatation of the pupil to 6 mm. in 40 minutes. The cycloplegic effect was at its maximum in 60 minutes, and was equal to that obtained from the use of either atropine or homatropine alone. The effect resulting from the use of homatropine and paredrine began to wear off in 4 to 5 hours, the eyes becoming normal within 18 hours. With atropine and paredrine the power of accommodation returns in from 2 to 3 days.

Tassman, I. S. (1938) *Amer. J. Ophthalm.*, **21**, 1019.

Irrigation of Posterior Chamber for Fundus Examination

For the examination and treatment of 3 difficult types of ophthalmic case, namely (i) patients with poor vision in whom the anterior segment of the eye is nearly normal but the fundus invisible, (ii) patients with poor vision in whom the anterior segment of the eye is diseased and the fundus invisible, and (iii) panophthalmitis, A. Motegi has evolved a technique for irrigating the posterior chamber with 0.9 per cent saline or Ringer's solution at body temperature. The conjunctiva is incised and the ocular muscles are resected; the sclera is then incised with the diathermy knife and a special thin cannula introduced into the vitreous space. Lavage removes pus and foreign bodies and allows a direct view of the fundus through the incision. A number of cases thus treated are reported, and it is stated that panophthalmitis in the early stages can be cured by intra-ocular irrigation.

Motegi, A. (1938) *Brit. J. Ophthalm.*, **22**, 543.

EYELIDS, INJURIES AND DISEASES

See also Vol. V, p. 239.

Warts

A. de Roth has seen in Hungary 10 cases of conjunctivitis or keratitis due to common warts of the margin of the lid. He estimated that the condition occurred in about 1 of every 3,200 cases of ocular disease. The patients were 7 females and 3 males between the ages of 13 and 80 years. The disease occurred 8 times on the left side and twice on the right, and de Roth reported an additional case in which both eyes were affected. The upper lid was involved more often than the lower. All the patients recovered in a few days after the removal of the warts. The clinical picture of most of the cases was that of subacute conjunctivitis, though one was acute and one follicular. The staphylococcus was the commonest organism present. In some cases the cornea was involved either as a superficial punctate keratitis or by ulcer formation. It is possible that the ulcer was secondary to the conjunctival infection. The disease resisted all the usual forms of treatment, but disappeared when the wart was removed, and it was therefore supposed that the virus of the wart caused the ocular condition.

Roth, A. de (1939) *Arch. Ophthalm.*, N.Y., **21**, 409.

FALLOPIAN TUBES DISEASES

See also Vol. V, p. 250.

Torsion

In the Virgin

Torsion of the uterine (Fallopian) tube is very rare in virgins, but the case of a virgin, aged 19 years, who developed this condition was reported by S. A. Wolfe and D. Kuperstein. The patient was admitted to hospital with pain in the lower left abdomen, which began three days before menstruation and persisted until two days after completion of the bleeding and had occurred monthly for about 9 months. There was a tender mass in the abdomen, dull to percussion, 2 to 3 cm. above the left inguinal (Poupart's) ligament. In the left fornix a cystic mass pushing the uterus over to the right was felt and thought to be an ovarian cyst, but on laparotomy it was found to be a twisted uterine (Fallopian) tube. The temperature, pulse, and respiration were normal. The tube was twisted with two complete turns at the

junction of the middle and outer thirds. The dilated ampullar segment was the seat of an old haematoma, and the wall was completely necrotic distal to the torsion. There was no sign of inflammation, and the opposite tube and ovary were normal. The left tube was untwisted, resected, and excised at its interstitial portion, but the left ovary was retained; the patient made an uninterrupted recovery

Wolfe, S. A., and Kuperstein, D. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 509.

Infections

Actinomycosis and Blastomycosis

M. Joseph and F. Summerill reported a case of actinomycosis of the right uterine (Fallopian) tube. The patient had fever with delirium after the birth of her child. This was followed by right-sided pain, nausea, and vomiting. The tubes, right ovary, and appendix were removed at operation, and the patient made a good recovery. Another woman aged 29 years complaining of pelvic discomfort, nausea, and vomiting, and having a normal catamenia was found at operation to be suffering from blastomycosis of the Fallopian tubes; these were removed with one ovary, and the patient made an uneventful recovery. The first patient was probably infected after her delivery and the second by extension from the appendix which could not be separately identified in the mass removed at operation.

Joseph, M., and Summerill, F. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 126

Tubal Pregnancy

Course and Prognosis

Sterility and fertility.—A series of 142 cases of ectopic pregnancy between 1926 and 1935 was considered by C. W. Mayo and E. O. Strassmann with special regard to subsequent sterility and fertility. Of the 142 one was an abdominal pregnancy and one an ovarian. In 77 of the remaining 140 the right tube was involved, and in 63 the left. It was thought that former inflammation of the appendix might be responsible in some cases for involvement of the right tube. In this series one patient came to hospital in a condition of profound shock, and died before operation was possible. Thirty-three patients became sterile as a result of operation, one as a result of X-ray irradiation, and 7 could not, for various reasons, be expected to become pregnant. In the remaining 100 cases, subsequent pregnancy was considered to be theoretically possible. Owing to difficulties in following up, reports could only be made on 84 cases. Thirty-one of these became pregnant, of whom 28 had intra-uterine pregnancies and 3 extra-uterine. There were finally 47 pregnancies in these 28 patients, 29 of which were normal full-time deliveries, and 3 still-births. There were 4 premature deliveries, 10 miscarriages, and one hydatidiform mole. Compared with an earlier series of cases observed from 1903-1926, the percentage of recurrences after operation for ectopic pregnancies dropped from 6 per cent to 3.6 per cent. The importance of conservatism in operative procedure is stressed, and the question as to whether such inflammatory changes as may be present in the non-pregnant tube will subside or become chronic must be decided by the surgeon. The fact should not be forgotten, however, that there is a higher mortality in recurrent ectopic pregnancies than in primary cases.

Diagnosis

Modification of Cullen's sign.—L. Brady describes a modification of Cullen's sign, — i.e. bluish discoloration of the umbilicus—as an indication of ruptured extra-uterine pregnancy. The discoloration in his case did not appear at or around the umbilicus or in a post-operative hernia, but in a thin spot in the abdominal wall which had developed as the result of an operation for ruptured appendix. The centre of the scar was bluish-black, and the surrounding area showed different hues of colour, such as are seen in a fading bruise. There was no hernia in the post-operative scar, and there was definite tenderness on palpation over the lower part of the abdomen. The author suggests that in future, when intra-abdominal haemorrhage is suspected, the Cullen sign should also be sought in any weak spots in the abdominal wall.

Brady, L. (1939) *J. Amer. med. Ass.*, **112**, 628.

Mayo, C. W., and Strassmann, E. O. (1938) *Surg. Gynec. Obstet.*, **67**, 46.

Gangrene of Hydatid of Morgagni

J. M. Waugh during 2 years had seen 3 cases in which accidents due to disease of the hydatid of Morgagni had caused abnormal symptoms, and has reported a case in an unmarried woman, aged 22, with pain in the right lower quadrant of the abdomen, tenderness over McBurney's point, and a leucocyte count of 12,000; there was no vomiting or diarrhoea, and menstruation was normal. As mild appendicitis was probable, laparotomy was performed; the appendix and gall-bladder were normal, but a strangulated hydatid hanging down from the fimbriated end of the right Fallopian tube was found. In 18 collected cases a correct pre-operative diagnosis had not been made, indeed there were not any characteristic signs of torsion, haemorrhage, gangrene, and rupture. On the right side appendicitis was imitated, on the left side a twisted ovarian cyst or extra-uterine gestation might be suggested. This lesion had been detected twice as often on the right side as on the left, because of the greater frequency of operation for abdominal emergencies on that side, but probably the small size of the hydatid accounted for the failure to detect it. The treatment was ligation of the pedicle, and excision.

Waugh, J. M. (1939) *Proc. Mayo Clin.*, **14**, 358.

FILARIASIS

See also Vol. V, p. 301, and Cumulative Supplement, Key Nos. 490-495.

Filariinae

Elephantiasis

Treatment—J. Knott treated 105 cases of filarial elephantiasis of the leg by prolonged firm bandaging which was effective in removing lymphoedema and gave the patient prompt symptomatic relief. Two out-patient methods of bandaging are described: the smaller legs were treated with the bandage boot—crepe bandage applied over towelling and with the turns of the bandage glued together with dextrin, the larger legs were bandaged with burlap bandages on which a lacing was sewed, tightening the lacing gathers the slack of the bandage into a tuck and produces firm compression. After the leg was reduced by bandaging, a legging was fitted. This method proved a great help to operative treatment, as the size of the leg and the lymphoedema can be controlled both before and after operation.

Knott, J. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 243.

Onchocercinae

Onchocerca volvulus

L. Déjou drew attention to arthritis in the large joints of the body caused by microfilariae (African onchocercosis). The diagnosis can easily be made by aspirating the joint and demonstrating the organism under the microscope. Natives of Togo, Dahomey, and the Fbony Coast are the principal sufferers, but, as the colonial army is often garrisoned in Europe, knowledge of this arthritis is of importance. The treatment advised by the author was repeated aspiration until the temperature, which is usually raised, became normal and the swelling had subsided.

Déjou, L. (1939) *Pr. méd.*, **49**, 983.

FOETUS DISEASES, MALFORMATIONS AND MONSTROSITIES

See also Vol. V, p. 334, and Cumulative Supplement, Key Nos. 503-512.

Abnormal Conditions in Living Foetus

Skin

Ehlers-Danlos syndrome—At a meeting of the Section of Dermatology of the Royal Society of Medicine on March 16th, 1939, 3 cases of the Ehlers-Danlos syndrome, i.e. laxity of the skin (cutis laxa), especially over the elbows and knees,

and liability for the skin to split and be long in healing, hyper-flexibility of the joints, and movable subcutaneous fatty 'spherules', were shown (Parkes Weber and Huber; Goldsmith; and Lowe). In none of the cases were the spherules certainly present. In Lowe's case there was congenital radio-ulnar synostosis on both sides and of the first degree, an association apparently now recorded for the first time. Parkes Weber referred to the association with a very striking trigeminal vascular naevus, and suggested that such developmental dysplasias would be more often described in cases of the Ehlers-Danlos syndrome.

Respiratory System

Nose. D. B. Kelly discusses the occurrence of congenital occlusion or atresia of the posterior nasal choanae, caused by a failure of absorption of the bucco-nasal membrane. It may be unilateral or bilateral, in structure either membranous or bony, or partly membranous and partly bony. It is generally accepted that the obstruction is due to the persistence of a vestigial epithelial structure—the bucco-nasal membrane—a partition between the mouth and the nose closing the posterior end of each olfactory pit in the embryo. When the condition is bilateral in babies it causes considerable difficulty in breathing, giving rise to severe dyspnoea and even to cyanosis, which are relieved only when the mouth is opened to cry. Sucking and consequently nutrition are also impaired. Unilateral cases are rarely recognized early in life. Relief is sought only when the patient is old enough to realize that one nasal passage is blocked, and there is a troublesome discharge of mucus, frequently resulting in excoriation of the upper lip. Diagnosis may be verified with iodized oil and X-ray photographs. Surgical procedure in the case of an adult consists of making an opening in the bony partition, by means of a long fine chisel passed through the left nostril, under a general anaesthetic. The edges of the obstructing plate are trimmed with a sphenoidal punch, and finally a portion of the posterior edge of the septum is removed with adenoid forceps. A rubber drainage tube is passed by the nostril through the ostium into the nasopharynx and retained in position for 24 hours. Often it is badly tolerated, and difficulty is experienced in maintaining the patency of the aperture. Experiments to overcome this difficulty have not met with permanent success.

Nervous System

Anencephaly.—Absence of the pituitary and of the adrenal cortex has often been found in anencephaly. On the other hand more recent observers have found both glands present, the adrenals sometimes being of the adult type. D. M. Angevine investigated this question in 20 anencephalic monsters. The anterior pituitary was always present, the pars intermedia in 6, and the pars nervosa in 5. In 18 cases in which they were examined, the adrenals also were always present and of the adult type. Angevine considered that prenatal atrophy had occurred in them; this atrophy may be due to lack of development in the pituitary. Examination of the thyroids, thymuses, ovaries, and testes in this series did not show any deviation from normal for the age of the foetus. In many cases the site of the cerebral hemispheres was occupied by haemorrhagic tissue in which the remains of the choroid plexuses were prominent. It was suggested that this large exposed plexus might, by adding cerebrospinal fluid to the amniotic fluid, play a part in the production of the hydramnios often present in these monsters.

- Angevine, D. M. (1938) *Arch. Path.*, **26**, 507.
 Goldsmith, W. N. (1939) *Proc. R. Soc. Med.*, **32**, 1027.
 Kelly, D. B. (1939) *Brit. med. J.*, **1**, 157.
 Lowe, J. (1939) *Proc. R. Soc. Med.*, **32**, 1027.
 Weber, F. P. (1939) *Proc. R. Soc. Med.*, **32**, 1028.
 — and Huber, H. (1939) *ibid.*, **32**, 1026.

FOOD

See also Vol. V, p. 388.

Inorganic Salts

Iron

That the intestine cannot regulate by excretion the amount of iron in the body has been shown experimentally by R. A. McCance and E. M. Widdowson. In the first stage of the experiment 3 men and 3 women were placed on diets containing 5.9 to

8.6 mg. of iron per day, and were shown to be in balance. In the second stage the daily intake of iron by the mouth was raised to 12 to 16 mg. per day, and the subjects were again shown to be in balance, all the additional iron being excreted. In the third stage 7 mg. of iron was injected intravenously daily, the intake by mouth varying from 7.7 to 11.7 mg. per day. None of the injected iron was excreted into the gastro-intestinal tract, the amount of iron in the faeces being in all subjects approximately that in the food. About 1.4 per cent of the iron was excreted in the urine, but this is almost certainly of no practical significance in iron metabolism. Since the subjects were known to be in iron equilibrium beforehand, and fully saturated with iron up to normal capacity, the injected iron should have been excreted into the intestine in recognizable amounts, if the intestine plays any large part in regulating the amount of iron in the body.

McCance, R. A., and Widdowson, E. M. (1938) *J. Physiol.*, **94**, 148.

FOOT, DISEASES AND DEFORMITIES

See also Vol. V, p. 412

Flat-Foot

Treatment

Surgical.—J. B. L'Episcopo and P. I. Sabatelle performed Hoke's operation on 16 patients, whose average age was 13 years, with flaccid flat-feet associated with pain, or fatigue, or both. Patients with arthritic symptoms were excluded. Both feet were operated on in each case. In 14 cases the first cuneiform and navicular were bridged by small bone grafts. In one case bone chips were placed between these 2 bones, and in another a wedge was removed from these bones, and their raw surfaces were brought together. The tendo Achillis was lengthened in 14 cases, but in the remaining 2 it was sufficiently long. The patients were allowed to walk in plaster casts with the aid of crutches 3 weeks after operation, but the feet were immobilized for an average period of 9 weeks. Whitman plates were applied when the casts were removed, and were worn for 2 to 12 months. The results were good in 11 cases, and fair in 5. There were no complete failures. X-ray examination showed that bony union was not essential for good results. Some patients obtained definite relief in spite of fibrous union.

L'Episcopo, J. B., and Sabatelle, P. F. (1939) *J. Bone Jt Surg.*, **21**, 92.

Hoke, M. (1931) *J. Bone Jt Surg.*, **13**, 773.

Painful Conditions

Treatment

Foot-roller.—E. Payr published a new method for the treatment and prevention of painful conditions of the feet, mainly affecting the os calcis and the sole of the foot. Oedema around the internal malleolus and pain in the calf muscles together with painful dorsiflexion characterized the early stages of thrombosis, and the author reviewed the anatomy of the foot which led him to devise a wooden roll, to be fixed transversely at the foot end of the bed, allowing it to rotate. The patients were instructed to put their sole on this roll and forcibly rotate it. The results were that this 'walk in bed' improved the general condition and acted as a sufficient stimulus to the sluggish circulation of the lower extremities. This therapy was then further used in different painful conditions of the feet and the results were, on the whole, very encouraging.

Payr, E. (1939) *Munch. med. Wschr.*, **86**, 580

FUNGOUS DISEASES

See also Vol. V, p. 448, Cumulative Supplement, Key Nos. 529–544; and p. 64 of this volume.

Ringworm of the Scalp

Kerion

According to M. Moore, kerion of the beard or scalp is still uncommon in the United States. Most cases have occurred on the east coast in large cities. In the

extremely few found in the Middle West, the tendency is towards kerion of the scalp. He reported the case of a male aged 42 years with a rapidly growing inflamed mass on his left chin of 10 to 12 days' duration; there was a reddish mass, about 2 cm. in diameter and 1 cm. above the skin surface, with an induration extending round the lesion for 3 cm. The kerion was incised and the escaping fluid caught in test tubes, and cultured. After a week the lesion showed crusts, and some days later X-ray irradiation was given. Some 3 weeks later the site of the lesion showed only a slight redness. The organism on culture developed at first colonies similar to those of *Ectotrichophyton mentagrophytes*.

Moore, M. (1938) *Brit. J. Derm.*, **50**, 653.

Ringworm of the Feet and Hands

Treatment

Sterilization of garments.—D. A. Berberian studied the infectivity and methods of prevention of dermatophytosis of the feet ('athlete's foot'). He took one washed and one unwashed stocking of a patient suffering from ringworm of the feet, and from both grew typical colonies of *T. interdigitale*, proving that simple laundering does not kill the fungus; the patient may therefore be reinfected from his own stockings, and the fungus can grow and multiply on the stockings in the presence of sufficient moisture. He also found that *T. interdigitale* would grow on silk, woollen, or cotton stockings and on the material commonly used by shoemakers for lining shoes. The stockings and lining materials used were then placed in a bedside cabinet with 10 to 15 c.cm. of commercial formaldehyde in an open dish, and the cabinet closed tightly. After 12 hours all the organisms on all the materials were destroyed, and Berberian suggested that this method of sterilizing the garments might be adopted by the patient. He also found that *T. interdigitale* would grow and multiply on wood, seaweed, and to a less extent on rocks covered with debris of dead moss and dirt. The condition is often contracted when swimming or diving off a board, since the swimmer may then be walking on cultures of fungi.

Sweat compounds.—S. M. Peck *et al* investigated the fungicidal power of normal sweat and of its components by testing its action on cultures of *Trichophyton gypsum*, *Epidermophyton inguinale*, and *Monilia albicans*. Dilute heat sweat did not inhibit the growth of *T. gypsum*. These same samples evaporated to dryness were fungicidal in a concentration ranging from 4 to 7 per cent. Two samples of sweat analysed contained propionic, acetic, and caprylic acids, sodium chloride, urea, and uric acid. One sample was found to contain 0.42 mg. per 100 c.cm. of ascorbic acid, and another sample 0.0862 mg. per 100 c.cm. An artificial sweat added to solid cultures was fungicidal. Addition of lactic acid to sweat caused inhibition of growth of the cultures. Dilute heat sweat may be fungicidal, if acid. Sebum from sebaceous cysts was not fungicidal. Of the individual components of sweat, butyric, propionic, formic, and acetic acids were fungicidal in greater concentration than the other components. In general, salts of the acids were less fungicidal than the acids. Fifty-one patients with various types of fungous infection were treated with lotions or ointments containing sodium propionate and other constituents of sweat; 24 were healed, 16 improved, and 11 not improved. The authors think that the distribution of fungous infections on the skin may be explained by variations in the composition of the sweat, that areas in which the sweat is concentrated have less tendency to infection than areas in which it is dilute, and that hyperidrosis favours fungous infection because the sweat in this condition is dilute.

Vaccines.—J. A. Tolmach and E. F. Traul undertook the treatment of dermatophytosis in 65 patients with 3 different vaccines, a heat-killed vaccine, an acid-killed vaccine, and dermatomycol, using no adjuvants. From the results it was considered that vaccine treatment in this condition is not yet practicable. Over 60 per cent of the patients were entirely uninfluenced by the treatment and, although 9 per cent showed apparent cure, it is pointed out that all dermatologists have encountered cases of apparent cure, regardless of the type of treatment, in which a recurrence appeared within a few days or weeks. With intradermal injections of fungus extract (trichophylin) the percentage of successes was raised to 10 per cent, and convalescent serum in a small series of cases produced a 28 per cent cure.

Surfer's Feet

H. L. Kesteven has made a comprehensive study of the flora found in cases of surfer's foot. In all, sixteen pathogenic fungi have been isolated, which are distri-

buted through the following genera: *Epidermophyton*, *Ectotrichophyton*, *Microsporon*, 'monilia', and *Eutorula*. In addition, the author states that a few aspergilli and two unidentified yeast forms have appeared in cases which are clinically pedal tinea, and are under suspicion. The condition, which has little relation with its name, appears to be mainly due to infected leathers. Treatment consists of the application of weak solution of iodine; or weak solution of iodine, compound tincture of benzoin and glycerin, in equal parts, or 48 hours' continuous treatment with eusol. It is necessary to continue routine application of the solution or paint used for 3 months after healing takes place, in order to prevent recurrent infection. Resistant recurring infections usually yield to a 1 per cent solution of dihydroxyanthranol (cignolin) in benzene.

Berberian, D. A. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 367.

Kesteven, H. L. (1939) *Med. J. Aust.*, **1**, 420.

Peck, S. M., Rosenfeld, H., Leifer, W., and Bierman, W. (1939) *Arch. Derm. Syph., Chicago*, **39**, 126.

Tolmach, J. A., and Traul, E. F. (1938) *Arch. Derm. Syph., Chicago*, **38**, 925.

GALL-BLADDER AND BILE-DUCTS

See also Vol. V, p. 477, Cumulative Supplement, Key Nos. 545 550, and p 48 of this volume.

Gall-Stones

Composition

A. T. Cameron *et al.* report on a calculous mass, removed by cholecystectomy, which weighed 8.41 g. It consisted of 91 small dark faceted stones, varying in size from a pin-head to a pea, and embedded in a yellow chalky material. The small stones were harder in consistence than the yellow matrix, and were examined separately. The yellow chalky matrix was composed of soft, friable material, yellow and homogeneous throughout. There was not any trace of concentric deposition. The material was insoluble in chloroform, boiling water, and hot glacial acetic acid. It dissolved in hot dilute hydrochloric acid and in 10 per cent acetic acid with evolution of carbon dioxide. In each case a yellow residue was left. Treatment of this residue with glacial acetic acid removed the yellow colour, but left a slightly green residue, suggesting bilirubin. Dilution of the glacial acetic acid extract did not produce any precipitate, indicating complete absence of fatty acids. The ignited material yielded much ash, containing calcium, phosphate, and an inestimable trace of magnesium, 79.3 per cent being calcium carbonate, calcium phosphate, and cholesterol. The number of such cases reported is steadily increasing and this form of deposit, though uncommon, is probably not extremely rare.

Clinical Picture

Causing intestinal obstruction.—In the opinion of R. M. Lowman and E. G. Wissing intestinal obstruction caused by gall-stones is comparatively rare. They quote a report of the British Medical Association that it accounted for 28 cases in a series of 3,000 intestinal obstructions. In none of these was the diagnosis made pre-operatively. Since the operative mortality varies between 40 and 50 per cent, early diagnosis is essential for success and preservation of life. It was suggested by the authors that such diagnosis should be established by X-rays in all cases of obstruction, except those with diffuse peritonitis. When gall-stones are present they are usually radio-opaque, owing to deposition of calcium, and the distribution of gas shadows is a valuable aid in detecting their presence. If gas is seen proximal to the stone, but is absent from the distal side, it is highly indicative of mechanical obstruction. A fistulous track between the gall-bladder and bowel may also be demonstrated by the barium sulphate meal. The authors quote a case in which multiple stones were found in the fundus of the gall-bladder, and one large stone lay transversely in the first portion of the duodenum.

Diagnosis

Stones in faeces.—M. Ortmyer and M. Austin presented 3 cases in which gall-stones, which had passed the sphincter of Oddi during attacks of pain in the right

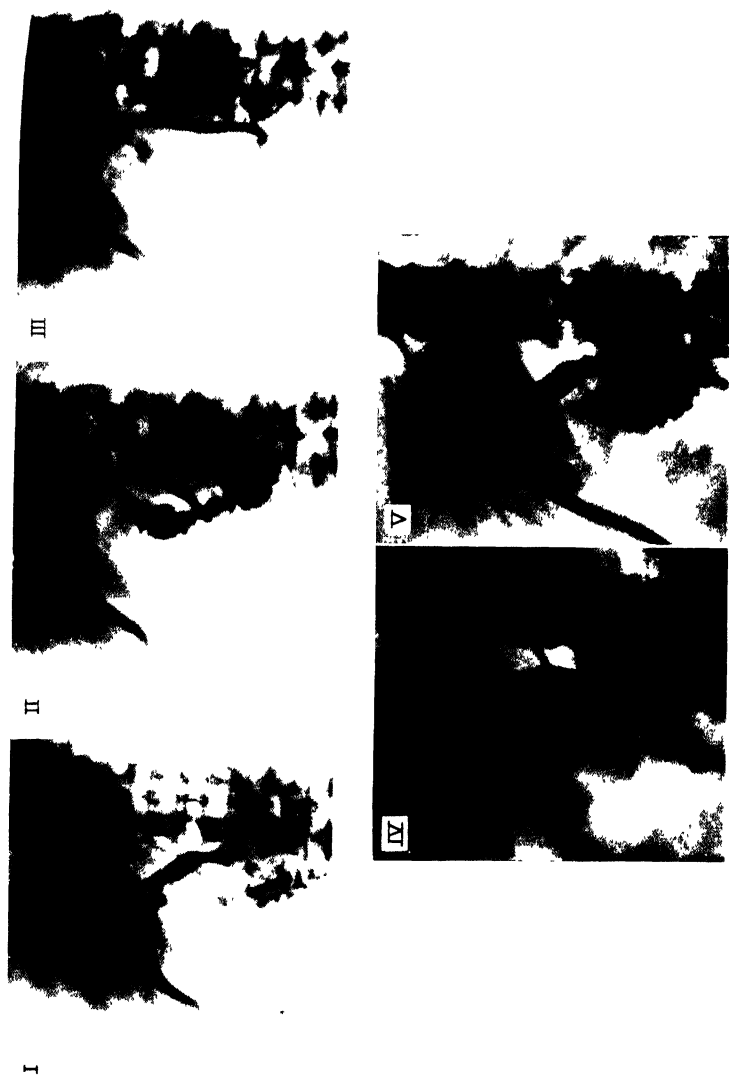


Figure 1
 I - Radiogram after iodized oil (lipiodol) showing gall-stone lying over the duodenal papilla
 II - Gall-stones dissolved after a fortnight's treatment with ether remaining pulp passed into the duodenum
 III - Drain introduced through the papilla into the duodenum
 IV - Gall-stones over the papilla
 V - Papilla freed after four weeks' treatment (From *The Lancet*, 1939)

upper quadrant, associated with jaundice were recovered from the faeces. It is pointed out that, although the passage of stones through the natural openings is comparatively common, this means of diagnosis is usually neglected. When the presence of a stone in the common duct is suspected, the oral administration of magnesium sulphate or other suitable drug may be tried as a means of evacuation into the duodenum, before surgical intervention is attempted. Care must be taken to ascertain that all stones are passed.

Urinary diastase.—It has been stated that the urinary diastase is raised in cases of stone in the common bile-duct. This led C. D. Branch and R. Zollinger to determine the blood diastase index in 75 cases of cholelithiasis; in this series there were 12 with stones in the common duct at operation, and, in 6 of these 12 cases, there was a definite rise in the blood diastase index, varying from 300 to more than 1,000 per cent. The diastase index was regarded as of value in the diagnosis of a stone in the common duct, provided that it was taken immediately after an attack of biliary colic; but on the whole the usual symptomatology and operative findings were still the most important diagnostic factors.

Treatment

Injection of ether.—B. O. C. Pribram injected ether into the common bile-duct to dissolve stones which had been impacted there. The mortality-rate of surgical interference in these cases is high, varying from 20 to 40 per cent, because the patient is often suffering from toxæmia or hepatic insufficiency. In addition the operation is often not a success, as some of the stones are overlooked, and give rise to further trouble. The author treated 38 cases of stones, which were so impacted that they could not be removed by the transduodenal route, by injection into the duct. The drain was introduced through the opening in the common duct right down to the stones, and held in position by catgut sutures, the hepato-duodenal ligament also being sewn round it (see Plate I and Fig. 13). The quantity of ether used depends on the width of the common duct. If large, the latter can take 0.5 c.cm. or 1 c.cm. The bile is sucked out of the drain with a syringe, so as to empty the duct. The ether is carefully injected drop by drop until epigastric pressure is felt. The injection may be repeated several times, and finally, after the injection of 1 to 2 c.cm. of liquid paraffin, the drain is closed with a clamp which the patient only removes when he again feels pressure. An injection of 50 c.cm. of a 33 per cent solution of magnesium sulphate can also be made, 2 or 3 times a week, through a duodenal tube. All the cases so treated were successful. The author also successfully treated biliary fistulae due to stones in the duct, which had been overlooked.

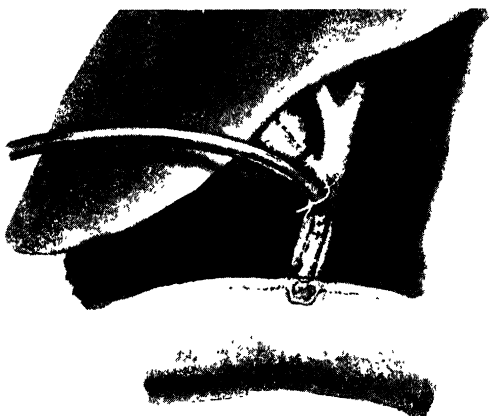


FIG. 13. Ether treatment of impacted gall-stones. Method of introducing the drain through the opening in the common duct and passing it as far as the stones in the ampulla of Vater. The opening in the common duct is sewn so as to be water-tight round the drain, which is held in place by binding the catgut sutures round it (From *The Lancet*, 1939)

- Branch, C. D., and Zollinger, R. (1938) *Amer. J. Surg.*, **41**, 233.
 Cameron, A. T., White, F. D., and Meltzer, S. (1938) *Canad. med. Ass. J.*, **39**, 441.
 Lowman, R. M., and Wissing, E. G. (1939) *J. Amer. med. Ass.*, **112**, 2247.
 Ortmyer, M., and Austin, M. (1938) *Amer. J. digest. Dis.*, **5**, 411.
 Pribram, B. O. C. (1939) *Lancet*, **1**, 1311.

Cholecystitis

Aetiology

Pancreatic reflux.—It has been shown experimentally that pancreatic juice introduced into the dog's gall-bladder can produce inflammatory changes, extending in some cases to necrosis and gangrene. It has also often been proved that there is an anatomical pathway between the biliary and pancreatic ducts. These facts led J. A. Wolfer to suppose that pancreatic reflux might be an aetiological factor in gall-bladder disease. He has shown that, in cholangiography, the pancreatic duct is often filled with opaque material, showing that a connexion between the 2 systems of ducts can exist. Also, when the common duct was drained in these cases, large amounts of amylase could be obtained from it. That the common duct is controlled by a sphincter is admitted by all observers. This sphincter may be acted upon by drugs, or upset by some change in its motor system. A stone impacted in the common duct, if it does not occlude the lumen of the pancreatic duct, will cause the pancreatic juice to enter the gall-bladder, spasm of the sphincter may do the same. The agent which activates the pancreatic juice has not yet been determined. It is suggested that it may be an enterokinase in the mucosa of the gall-bladder, or derived from a micro-organism. That it is not the bile has been proved.

Lesions of cystic duct. W. H. Cole and L. J. Rossiter review the possibilities of the relationship of lesions of the cystic duct to gall-bladder disease, and give a full description of the anatomy and effect of pathological processes on the physiology of the cystic duct. They find that an important feature of lesions of the cystic duct is that they are usually congenital, but do not produce symptoms until late in life when inflammatory processes are prone to manifest themselves. The lesions which are most likely to cause partial obstruction of the cystic duct are adhesions and kinks, inflammatory processes which may involve the valves of Heister, stone in the duct; and pressure from extrinsic tumours or enlarged lymph glands. It is demonstrated by a survey of 7 cases, treated by cholecystectomy, that the lesion in the cystic duct is frequently the only significant lesion of the gall-bladder, or may be the instigating factor of disease in the gall-bladder itself. It is difficult to form an opinion of the degrees of obstruction existing in the cystic duct. It would scarcely be justifiable to perform tests for this purpose while the patient was under an anaesthetic, prior to excision. The authors have observed that, in some instances, failure of the gall-bladder to empty following a meal rich in fats is indicative of serious cholecystic disease.

Morbid Anatomy

To show the frequent association of hypertrophy of the smooth muscle of the gall-bladder with chronic cholecystitis and cholelithiasis, K. B. Lawrence and S. Warren examined 100 gall-bladders removed at operation, all of which showed some cholecystitis; 50 normal gall-bladders obtained at necropsy were used as controls. The average thickness of the muscular layer of the normal gall-bladders was 0.16 mm., and that of the surgically removed gall-bladders 0.54 mm. The Rokitsansky-Aschoff sinuses, or mucosal diverticula, often found in thickened gall-bladders, were present in 60 of the 100 diseased gall-bladders, but in only 3 of the normal 50. These sinuses had been ascribed to powerful contractions of the viscus due to repeated over-distension. Microscopically the increased thickness of the gall-bladder appeared to be due to hypertrophy of the smooth muscle fibres, but no satisfactory explanation of the cause of this hypertrophy was available.

Prognosis

After operation.—S. G. Meyers *et al.* studied for an average period of seven and a half years after operation a series of 165 patients, who had had 199 operations for biliary tract disease. It was found that 83 per cent of those with calculous cholecystitis benefited from operation, but only 41 per cent of those with non-calculous cholecystitis. From the prognostic point of view the least favourable group was that in which no pre-operative colic was present and no stones were found. The chief causes of recurrent symptoms of biliary tract origin included stones in the common and in the cystic duct. Residual biliary indigestion, biliary dyskinesia, and the so-called convalescent biliary colic, which arises from the loss of the reservoir function, thus causing compensating dilatation of the larger bile-ducts and derangement in emptying time, are cited as common post-operative causes of recurrent symptoms. Amongst extra-biliary causes are intestinal adhesions, spasticity of the colon, peptic ulcers, and anxiety neuroses.

M. J. Brown studied 346 uncomplicated cases of non-calculous chronic cholecystitis, 256 in females and 90 in males. Most of the patients were suffering from cholecystitis or cholesterosis. The symptoms were upper abdominal pain, nausea, vomiting, flatulence, constipation, and radiation of pain to the right shoulder and back. Cholecystographic examination showed delayed emptying of the gall-bladder in most cases. The mortality rate for 320 cholecystectomies was 2.8 per cent, whereas there was no fatality in 26 cholecystostomies. Hepatitis and adhesions were found in many of the cases. About half the patients obtained relief from cholecystectomy, notably those in whom adhesions were present. Brown concluded that patients with non-calculous gall-bladder disease should not be submitted to surgery until a careful differential diagnosis has been made, and a period of intensive medical treatment has been tried.

Treatment of Post-Operative Syndromes

Bile salts and diet. H. Doubilet *et al.*, under the heading bile-salt therapy in gall-bladder disease, described the treatment of 3 forms of gall-bladder disease by (a) a diet low in fat, low in carbohydrate, high in protein (lean meat), vegetables, fruit, plenty of water, 3 meals daily, and no food between meals, and (b) bile salts in quantities from 15 to 60 gr. daily given during meals. As gastric irritation was sometimes due to large quantities of plain bile salts, an iron salt of ox-bile acids in a purified form was used. The average dose given daily was 15 to 45 gr. in capsules divided between the 3 meals. The therapeutic index employed to determine the dose was the control of constipation: all cathartics were stopped, and the amount of bile salts given was gradually increased from 5 gr. at each meal until the bowels acted at least once and not more than twice daily, this stabilization usually took about 2 weeks. Three groups of gall-bladder disease were thus treated, but it was clearly stated that this treatment was not suitable for obstructive jaundice, stenosis of the ducts by malignant disease, calculi, or chronic pancreatitis. (1) The post-cholecystectomy syndrome, pain, dyspepsia, and constipation: all but 1 of 13 patients were relieved from dyspepsia and constipation, 6 became free from pain, and in 4 pain was much diminished. (2) 14 cases of functioning gall-bladders containing gall-stones, as shown radiologically: all were relieved from dyspepsia and constipation, 8 became free from attacks of pain, and 4 were much improved in this respect. (3) 11 patients with non-visualized gall-bladders were, as in the previous groups, relieved from dyspepsia and constipation, and 8 patients were rendered free from pain. In patients with hyperacidity atropine and alkalis were a useful adjuvant.

Brown, M. J. (1938) *Amer. J. Surg.*, **41**, 238.

Cole, W. H., and Rossiter, L. J. (1938) *Amer. J. digest. Dis.*, **5**, 576.

Doubilet, H., Yarnes, H., and Winkelstein, A. (1938) *Amer. J. digest. Dis.*, **5**, 348.

Lawrence, K. B., and Warren, S. (1938) *Arch. Path.*, **26**, 449.

Meyers, S. G., Sandweiss, D. J., and Saltzstein, H. C. (1938) *Amer. J. digest. Dis.*, **5**, 667.

Wolfe, J. A. (1939) *Ann. Surg.*, **109**, 187.

Cholangitis

Treatment

Prontosil.—F. Kazda used prontosil in 6 cases of inflammation of the bile-ducts. In severe cases of cholangitis, cholecystitis, and pericholecystitis cure was definitely accelerated. The temperature returned to normal, jaundice disappeared, and the leucocyte count fell in one case from 10,600 to 5,200. The drug used was prontosil, and the dosage was 1 to 2 tablets of 0.5 g. 3 times a day for 5 days, or 1 to 2 injections of 5 c.cm. intramuscularly or intravenously. Prontosil was recommended during the pre-operative period in patients who should not be operated because there is acute inflammation.

Adrenal hormone.—T. v. Uexküll treated with adrenal hormone 4 cases of severe cholangitis with damage to the liver. Case 1: A woman aged 38 suffered from icterus, vomiting, pain, fever, and chills. She received 5 mg. per cent bilirubin in serum (choleval) and prontosil with no success. There was a rapid change of her general condition after intramuscular injections of 5 c.cm. of adrenal hormone (cortidyn). Case 2: The symptoms were similar. Liver function was disturbed. Insulin-glucose injections did not improve the condition; 5 c.cm. of cortidyn improved the condition, and the liver function test (galactose) also showed improvement. Case 3: The galactose test showed liver damage; 5 c.cm. of cortidyn was given for 6 days. The

temperature decreased from 39° to 37.5° C. (102.2° to 99.4° F.). The galactose test was still pathological, but improved. Case 4: The symptoms were very severe, and the general condition bad. The liver was enlarged and hard. Cortidyn for 4 days and then for 6 days caused improvement of the general condition and gain in weight.

Surgical.—C. W. Rosgen defined cholangitis as an infection of stone-free bile-ducts, through either the lymphatic or blood vessels or the intestine. Symptoms were pain in the area of the liver, vomiting, headache, fever, loss of weight, and icterus. The author operated on 13 patients with cholangitis, most of whom gave a history of dyspeptic symptoms. Three patients who had icterus of 3, 5, and 7 weeks' duration respectively died, two of them 4 days after operation and the other the day following the operation. Death was presumably caused by irreparable damage to the liver tissue. After operation the patients were given 'liver-protection treatment' with glucose and insulin, and recovered quickly. If medical treatment is protracted, it may be too late for surgical treatment because of the damage to the liver tissue.

Cholangitis Lenta

O. H. P. Pepper reported, under the name cholangitis lenta, a condition on which there had not been any previous contribution in English, though it has been described in Germany and Italy. It is a non-suppurative infection, usually streptococcal, of the bile-ducts, with signs of slow sepsis, splenomegaly, and other analogies with subacute bacterial (lenta) endocarditis. It, however, differs from the cardiac infection in being less fatal, some patients recover and others pass into biliary cirrhosis. It is probably an ascending infection of the bile-ducts. Pepper's case emphasized the analogy with endocarditis lenta, for the patient developed, on an old rheumatic valvulitis, an acute ulcerative endocarditis which in many respects resembled the condition formerly called endocarditis lenta. At the necropsy, the 2 processes—in the bile-ducts and in the heart—were confirmed.

Kazda, F. (1938) *Wien. klin. Wschr.*, **51**, 1099.

Pepper, O. H. P. (1938) *Trans. Coll. Phys., Philad.*, 4 ser., **6**, 39.

Rosgen, C. W. (1939) *Dtsch. med. Wschr.*, **65**, 641.

Ueskuhl, T. v. (1939) *Dtsch. med. Wschr.*, **65**, 509.

GLANDULAR FEVER

See also Vol. V, p. 559.

Clinical Picture

J. R. Paul analysed the clinical features, in 51 cases at the New Haven Hospital, Connecticut, of infectious mononucleosis, a title he preferred to glandular fever. Often the disease, which lasts 10 to 21 days, was an institutional malady of young adults, especially medical students, two-fifths of the 51 cases being associated, directly or indirectly, with the New Haven Hospital and those in sedentary occupations. The onset was insidious with sore throat, pain in the shoulders and neck, leucopenia, and irregular fever, it might imitate typhoid fever. At the end of the first week the lymphatic glands might be sufficiently enlarged to attract attention. Ocular symptoms were probably more often present than was generally recognized—pain in the eyes in the early stage, leaving some temporary swelling of the eyelids. A papulo-macular rash was irregularly present, and was described as morbilliform. Jaundice occurred in 10 per cent of the cases. During the first week half the cases showed leucopenia, due to granulocytopenia, the lymphoid cells rising from 28 to 68 per cent. In the second week there was a leucocytosis of from 8,000 to 20,000, the lymphocytes being from 40 to 85 per cent. By the end of the third week the total leucocyte count and the percentage of lymphoid cells fell. The red-cell count was unaltered throughout the disease. The characteristic heterophil or heterogenous antibodies, lysins and agglutinins, for sheep's red-cells were well in evidence during the second and third weeks, and were positive in 90 per cent of the New Haven cases. Temporary positive Wassermann or Kahn tests were present in 3 out of the 8 New Haven cases tested.

Paul, J. R. (1939) *Bull. N. Y. Acad. Med.*, 2 ser., **15**, 43.

Diagnosis

W. Saphir reported a case of infective mononucleosis in a woman of 32, which resembled the pre-eruptive stage of primary syphilis, and in which the Wassermann

and Kahn reactions were four-plus positive. She had the usual fever, malaise, and enlargement of the lymph glands and spleen. Later in the course of the disease she developed a maculo-papular rash. The heterophilic antibody test was positive. She recovered after 3 months of treatment, and a week following discharge the Wassermann and Kahn tests were completely negative. Of 30 other cases considered, only 2 had a temporary one-plus Wassermann reaction. The reason why infective mononucleosis should sometimes be associated with a positive Wassermann reaction is unknown, but Saphir suggested that it might be due to a disturbance in the protein fractions of the serum giving a non-specific protein reaction as is sometimes seen in malaria, pneumonia, and pregnancy.

F. A. Marshall reported 4 cases of infective mononucleosis. None of the cases showed the characteristic symptoms and signs. In one case cerebral symptoms predominated, in another, acute leukaemia was simulated, in the third, the disease appeared to be follicular tonsillitis, and in the fourth, weakness was the predominating symptom. All the cases gave a positive agglutination test for the presence of heterophil antibodies in the blood which is specific for mononucleosis. The author suggested accessory methods of diagnosis such as biopsy of a gland or differential blood counts, stressing the importance of accuracy, because the disease may simulate other conditions as shown in the above cases.

J. F. Sadusk recorded the experience of Bernstein who found that, among 60 cases of glandular fever observed at the Johns Hopkins Hospital during the past 5 years, 6 showed false positive serological reactions for syphilis. Of the 60, 37 had been given routine Wassermann tests. The positive reactions may occur in the first week of the condition. These become negative between the third and the seventh week, though in one case a positive result lasted until the tenth. No convincing reason has been advanced for these false reactions. The author has had 46 cases of glandular fever under his care in 17 years. Of the 37 tested by the Kahn and Wassermann reactions, 3 gave temporary positive results.

Subcutaneous injection of an emulsion, made from the lymphatic glands of cases of glandular fever, into three monkeys produced in two of them an illness like glandular fever in man after 8 and 18 days. A laboratory worker pricked his finger in operating on an injected monkey, and in spite of free bleeding from, and application of iodine to, the wound presented the symptoms of glandular fever 7 days later. Histologically the lymphatic glands of human patients with glandular fever were found by P. J. Wising to contain extracellular and intracellular granules resembling the 'elementary bodies' described by Paschen.

Marshall, F. A. (1939) *Amer. J. clin. Path.*, **9**, 298.

Sadusk, J. F. (1939) *J. Amer. med. Ass.*, **112**, 1682.

Saphir, W. (1939) *Amer. J. clin. Path.*, **9**, 306.

Wising, P. J. (1939) *Acta med. scand.*, **98**, 328.

GLAUCOMA

See also Vol. V, p. 575, and p. 129 of this volume.

Aetiology

P. Weinstein, in an analysis of 3,254 cases of glaucoma seen during 30 years, found that 23 per cent were emmetropic, and 15 per cent myopic, in contrast to the usual presumed association of glaucoma and hypermetropia, 60 per cent were females and 80 per cent of the acute attacks were in women at the time of the climacteric. Inflammatory glaucoma is rare in grave arteriosclerosis, nephrosclerosis, and diabetes mellitus. The ocular tension in those disposed to glaucoma is increased by several millimetres, compared with the normal, when they drink a large amount of liquid and after taking beverages containing caffeine (coffee, tea), or are in a position with their head low. The ocular tension of glaucomatous persons considerably increases after inspiration of amyl nitrite, whereas the ocular pressure of arteriosclerotics does not increase or only to an insignificant degree in similar conditions. The endocrine dysfunction of glaucomatous persons exerts its effect by disturbing the balance between the osmotic pressure of the blood proteins in the capillaries and arterioles, and the ocular tension.

Weinstein, P. (1939) *Brit. med. J.*, **1**, 436.

Treatment

Mecholyl

S. T. Clarke, in a comprehensive review of the drugs employed in the treatment of glaucoma, discussed the use of mecholyl (acetyl- β -methylcholine chloride) and prostigmin. Mecholyl has several valuable non-ophthalmological uses, such as in peripheral vascular disease, in paroxysmal tachycardia, in post-operative intestinal and urinary complications, and in arthritis. It is a white crystalline substance freely soluble in water. It cannot be used intravenously. It is a direct antagonist to adrenaline and atropine, contracting the pupil, lowering the blood pressure, increasing the heart rate, and constricting the bronchioles. Its general effect comes on within 2 minutes and passes off after 20. Its general effect may be instantly abolished by means of $\frac{1}{10}$ gr. of atropine sulphate given intravenously. In acute and subacute cases of glaucoma a 20 per cent solution as drops was tried, retrobulbar injection being found preferable to subconjunctival. It was found to produce a much more rapid and much greater fall in intra-ocular tension than adrenaline. 1 or a healthy adult 0.03 g. is the maximal dose and in elderly patients 0.010 g. is the minimal dose. Prostigmin, though resembling eserine in its action, has a stronger miotic effect, and is not so unpleasant. Though used in twice as strong a concentration it causes less general reaction such as nausea.

The author recommended as a good routine treatment for acute congestive glaucoma morphine $\frac{1}{4}$ gr. subcutaneously if much pain is present; mecholyl 20 per cent, prostigmin 5 per cent, one drop of each, given every 10 minutes for 7 doses; if the intra-ocular tension had not approached normal within one-and-a-half hours, a retrobulbar injection of 0.025 g. of mecholyl in 1 c.cm. of 2 per cent procaine hydrochloride should be given with continuation of the previous drops for another 5 doses. When mecholyl was used by the retrobulbar method in acute glaucoma tension was frequently brought to normal in 2 to 20 minutes.

Intravenous Injection of Sorbitol

Osmotic therapy has been used in the treatment of glaucoma. The injection of hypertonic saline is attended by pain, the risk of sloughing at the site of injection, and a secondary rise in intra-ocular tension if extravasated into the tissue to a level higher than the initial one present in the glaucoma. These dangers are present if glucose is used, together with the disadvantage that it cannot be used for diabetics. J. Bellows *et al.* found that 100 c.cm. of a 50 per cent solution of sorbitol (a complex alcohol of approximately the same molecular size as dextrose) given intravenously and repeated in 24 hours, if necessary, nearly always reduced intra-ocular tension when it was greatly increased and not controlled by the use of miotics alone. Because of its slight diffusibility, a secondary rise in tension above the initial value was not observed. It was useful in relieving the pain of glaucoma and in preparing the eye for operation.

Surgical

In the surgical treatment of glaucoma in the course of epidemic dropsy E. O'G. Kirwan has substituted for Elliot's sclero-corneal trephining operation an anterior sclerectomy, which is a modification of the Lagrange operation. In 192 operations by the modified Lagrange technique, Kirwan has not seen the late serious complications that follow Elliot's operation (e.g. a low form of iridocyclitis and secondary cataract). The technique consists in turning down a conjunctival flap under local anaesthesia. The surface of the sclera is exposed right up to the limbus. A small keratome is now introduced at a distance of 2 mm. from the limbus into the anterior chamber. The aqueous humour is allowed to escape very slowly. The upper margin of the wound is depressed, allowing the root of the iris to present. A small button-hole iridectomy is performed. With a little massage, the iris springs back into position. With a pair of scissors curved on the flat, a small sclerectomy is done, the portion of the sclera cut off being 1 to 1.5 mm. in height and 2 to 3 mm. in breadth. The conjunctival flap is then turned back and stitched up with a continuous suture, which is removed on the fifth day. The eye is dressed on the third morning and a drop of 1 per cent atropine put in. There is usually very little reaction. In this operation the filtering cicatrix is flat and does not encroach on the cornea, as in the Elliot trephine operation. Lagrange's advice (1937) should be remembered: 'Do not touch the cornea, for it proliferates, and do not touch the ciliary body, for it is resentful'.

Spleen Extract

E. A. Miller, working in conjunction with Paul, concluded that glaucoma was an angioneurotic oedema which developed within the eyeball and pressed against the inelastic sclerocorneal envelope. On the assumption that spleen extract removed allergic obstructions, as evidenced in cases of asthma, dysmenorrhoea, and migraine which had responded to this treatment originally given in these cases for eczema and urticaria, patients suffering with glaucoma received injections. The author treated 22 cases by this means. They all showed favourable results and some attained complete recovery. Dosage employed by the author was 20 c.cm. of the extract, 10 c.cm. being given in each upper arm, as an oedema may be produced if the whole 20 c.cm. is injected into one arm. The need is emphasized, however, for biologically standardized extracts, as none of those on the market can be satisfactorily compared with each other in regard to concentration. Some immediate reaction may be expected from this treatment, but this is transient. Alcohol is prohibited, as even the smallest quantity neutralizes the effect of spleen extract. Injections are given at 48-hour intervals unless symptoms reappear earlier, and may be continued for long periods, if necessary, without harmful effects. It is sometimes necessary to reduce the interval to every 12 hours. The only danger which may attach to the use of this therapy in glaucoma is the possibility of increasing the tension and intensifying the symptoms after the first injection. In 600 cases of asthma, angioneurotic oedema, urticaria, and eczema, only 2 per cent have reacted in such a manner.

Bellows, J., Puntenney, I., and Cowen, J. (1938) *Arch. Ophthalm.*, **N.Y.**, **20**, 1036.

Clarke, S. T. (1939) *Amer. J. Ophthalm.*, **22**, 249.

Kirwan, L. O'G. (1938) *Indian med. Gaz.*, **73**, 654.

Miller, E. A. (1939) *Amer. J. Ophthalm.*, **22**, 536.

GLYCOGEN DISEASE

See also Vol. V, p. 586.

Aetiology

In a monograph of 128 pages S. Van Creveld exhaustively analysed the reported cases, at least 50, and the various views put forward, especially about the causation, of glycogen disease or hepatomegalia glycogenica, since the first clinical case was described in 1928 by him. It has often been called von Gierke's disease from the account given by the Berlin professor in 1929 of hypertrophy of the liver and kidneys due to accumulation of glycogen (hepato-nephromegalia glycogenica). In this congenital disorder of glycogen metabolism, glycogen could only be mobilized with great difficulty, as shown during life by a poor response to injections of adrenaline, and by the great stability of this glycogen in the organs after death. In the liver the glycogen accumulation might be accompanied by fatty change. In some cases there was cardiomegalia glycogenica in which there was seldom also present the glycogenic infiltration of the liver and kidneys. This cardiac accumulation of glycogen might explain the so-called idiopathic hypertrophy of the heart in children. It was also concluded that cases reported as congenital diffuse rhabdomyoma of the heart were really examples of glycogen heart in which the increase was enormous and the muscular fibres were so extensively occupied by glycogen as to be almost unrecognizable. Cases of hepatomegalia glycogenica must be diagnosed clinically from cirrhosis of the liver and especially from congenital hypertrophic steatosis of the liver which may be a familial disease. The cases of the conditions were analysed, and the suggestion that there might be a *hépatomegalia polycorrique* (πολύς, much, and κόρος, saturation), or a combined pathological accumulation of 2 reserve substances—glycogen and fat—was contested. In this connexion it might be mentioned that von Gierke compared the glycogen disease with those conditions due to retention of other metabolic products—Gaucher's disease (kerasin) and Niemann-Pick disease (lipoids); the same might be suggested about haemochromatosis (iron). Von Gierke suggested a complete or partial absence of glycogen-splitting ferments. Absence of diastase in the liver and an abnormal binding of glycogen were other unacceptable hypotheses to explain the stability of glycogen. The endocrine glands, especially the anterior pituitary, had been suggested as primarily responsible for glycogen disease, and especially over-production of the

ketogenic principle. The suggestion that glycogen disease was due to hyperinsulinism—the reverse of diabetes mellitus—was rejected. According to Van Creveld the conception that there was an absence of a factor which normally interacts between the glycogen and the glycogen-splitting ferment had become more and more probable. There was a general agreement that the prognosis of glycogen disease, especially of the hepatic form, was good, and certainly there had been few necropsies. There did not appear to be any good reason for the statement that there was an increased liability to infections. There was not any definite treatment for glycogen disease. In the presence of hypoglycaemia with acetonuria, a diet predominantly carbohydrate and poor in fat had been adopted. Several hormones had been tried—thyroid, gonadotrophic, anterior pituitary, and adrenaline. The effects of X-irradiation were conflicting, and Van Creveld gave choline a long trial and considered that the excretion of ketone bodies was thereby much diminished.

Van Creveld, S. (1939) *Medicine, Baltimore*, **18**, 1

GLYCOSURIA

See also Vol. V, p. 593, and Cumulative Supplement, Key Nos. 567 and 568.

Aetiology

A. H. Neufeld and J. B. Collip conducted experiments, using fed rabbits of from 2 to 3 kg., to ascertain the pituitary factor antagonistic to adrenaline hyperglycaemia. The results made it clear that this factor originates in the posterior lobe. It was found to be stable to short heat treatment in an alkaline medium, but it was removed by prolonged heating in an acid medium. The factor responsible for stimulating metabolism was stable in both alkaline and acid heat treatment. It was soluble in a fairly high concentration of alcohol, and insoluble in ether; it was stable to both trypsin and pepsin digestion. It was concluded that the antagonistic factor was distinct from oxytocin and vasopressin, but the mechanism of the antagonism was not clear.

Neufeld, A. H., and Collip, J. B. (1939) *Canad. med. Ass. J.*, **40**, 537.

Differential Diagnosis

R. S. Hart and L. F. Wise published a case in which the first morning specimen of urine reduced Benedict's solution, although the blood-sugar was normal. For a month before the urine was first examined, the patient had been taking 6 mg. of thiamin chloride daily. Morning specimens from 3 other patients who were taking at least 6 mg. of thiamin chloride daily were examined, but did not show reduction of Benedict's solution. Possible explanations are (i) storage of thiamin chloride with marked elimination at intervals, and (ii) lowering of the renal threshold to dextrose through the agency of thiamin chloride. Pure thiamin chloride reduces Benedict's solution.

Hart, R. S., and Wise, L. F. (1939) *J. Amer. med. Ass.*, **112**, 423

GOITRE AND OTHER DISEASES OF THE THYROID GLAND

See also Vol. V, p. 599, and Cumulative Supplement, Key Nos. 569-574

Toxic Goitre

Aetiology

R. Sanchez-Calvo examined the various factors influencing the action of the thyroid gland. Light, darkness, temperature, and nutrition all play a part, but it has not hitherto been discovered what effect movements of the neck, notably forced stretching, has on the action of the gland. By experimental investigations on guinea-pigs the author was able to show that prolonged stretching of the neck over 4 to 48 hours produced hyperthyroidism. The contraction of the muscles, and cold, produced adrenalinaemia, which seemed to be the decisive factor.

R. Daniel, while regarding some of the hypotheses put forward to explain the causation of exophthalmos, such as an accumulation of fat and contraction of Müller's muscle, as inadequate, brings forward suggestions in favour of oedema in

the orbit. It is argued that increased muscular activity may cause an excess of tissue fluid, and that the main orbital veins may be pressed up by the much enlarged intra-orbital muscles, and that the apparent absence of any lymphatics in the orbit may play a part. In the discussion of this paper R. M. Wilder described two forms of exophthalmos in toxic goitre; (i) the less common occurs among patients with a low metabolic rate, after thyroidectomy, or after spontaneous remission of hyperthyroidism; it is called paradoxical and malignant because it is prone to lead to destruction of the globe; and (ii) the more common form running parallel with metabolic rate does not tend to destroy the eye

Clinical Picture

Masked symptoms.—E. P. Scarlett described 3 groups, with illustrative cases, of masked hyperthyroidism. (i) Cases in which the symptoms and signs related to one system were prominent, thus producing a clinical picture simulating disease of one system only. The most frequent form was the cardiac, usually in women over 40 years of age, with a palpable nodular goitre, with a history of mild cardiac failure for months or years, and repeated attacks of auricular fibrillation. Another type of case in group (i) was characterized by neuromuscular manifestations—weakness and tremor, in elderly patients with an adenomatous goitre, most of the ordinary symptoms of toxic goitre being absent. In group (ii) were patients, chiefly women past middle age, with a nodular goitre, gastro-intestinal symptoms, such as vomiting and diarrhoea, and with a low-grade fever. In this group came the cases Lahey described as 'apathetic hyperthyroidism', occurring in or after middle age, with a pulse rate of 90 to 120, a small firm thyroid, dry cool pigmented skin, an appearance of age above the actual, a dull facies, and a relatively low basal metabolic rate. In a third group there were cases of hyperthyroidism complicated by another condition which dominated the clinical picture viz hypertension, organic heart disease, menopausal symptoms, and diabetes mellitus. A distinct group of hypothyroid cases has a basic metabolic rate of 10 to 20 per cent, nervousness, chronic nervous exhaustion, fatigability, and constipation.

Oedema and jaundice.—F. Tiemann drew attention to the origin of oedema and jaundice in hyperthyroidism. It was widely held that this oedema and icterus were due to involvement of the heart. The author was able to show, however, that a serous hepatitis developed in the course of hyperthyroidism or toxic goitre, which was influenced by X-ray therapy and Lugol's solution.

Iodine content of blood and urine.—Extensive studies have been undertaken by I. D. Puppel and G. M. Curtis on the iodine content of the blood and urine in normal persons and in patients with exophthalmic goitre. In three normal persons, who were maintained on a low iodine intake averaging 87 mg. per 3-day period for 24 days, the iodine balance remained negative. The available data showed that, in normal persons, a certain amount of iodine is excreted daily over a yet undetermined period of time, regardless of the amount of iodine ingested. When iodine was given in excess of the amount excreted daily, there was a positive iodine balance.

Three patients with exophthalmic goitre, who were maintained on a low iodine intake, showed considerable increase in iodine excretion, particularly through the faeces. Two patients with exophthalmic goitre who were maintained on an intake of iodine sufficient to give a positive iodine balance in a normal person, showed a negative iodine balance.

Associated myasthenia gravis and hyperplastic thymus. Hyperplasia of the thymus was observed by H. Adler in about 50 per cent of cases of myasthenia gravis, and this gland was removed in several cases with good results. In dogs, transplantation of juvenile thymus as well as injection of thymus extract produced the symptoms of myasthenia gravis. These observations indicate that the internal secretion of the thymus influences striated muscles. As hyperplasia of the thymus was observed in many cases of toxic goitre, Adler examined the striated muscles in patients with this affection. The myasthenic reaction was often positive. Complete ophthalmoplegia externa, observed in one case of toxic goitre, disappeared for several hours on injection of prostigmin. Other symptoms of toxic goitre also certainly result from myasthenia gravis, for example the so-called 'thyrotoxic crisis' in which all striated muscles become paralysed. The significance of hyperfunction of the thymus in cases of toxic goitre has not yet been found. Probably hyperfunction of the thyroid gland causes hyperfunction of the thymus. The results of operations by Haberer seem to indicate the advisability of reducing the volume of the thymus in every case of toxic goitre.

In children.—F. R. B. Atkinson analysed 208 collected cases of toxic goitre under 15 years of age, the incidence rising progressively from 7 per cent in the first 2 years of life to 31 per cent in the age-period 12 to 14 years. Only 7 cases occurred during the first year of life. Tachycardia was the most frequent symptom, being present in all but 3 of 176 cases in which its presence or absence was mentioned; next came thyroid enlargement in 97 per cent of 192 cases, exophthalmos in 84 per cent, and tremor in 80 per cent. The prognosis seemed to be more favourable than in adults, as 6 fatal cases only were recorded.

Treatment

E. Ginsberg describes the treatment of 115 patients with toxic goitre. Various methods of treatment were used over a period of 2 to 6 years. Twenty-five patients were treated by 'lumbar blockade' according to the method of Speransky and Vishnensky, being given one or two injections of 100 c.cm. of 0.25 per cent solution of novocain (procaine hydrochloride). Others were given 12 to 15 applications of diathermy, one electrode being placed from the fourth cervical to the second thoracic vertebra, and the other electrode on the lumbo-sacral region of the spine. Another group of patients were given 8 or 9 erythema doses of ultra-violet light to the lumbar region at intervals of 4 days. None of these patients suffered from toxic adenoma. The types of treatment mentioned gave subjective improvement in all cases. There was noticeable improvement also in the cardiovascular symptoms, in the exophthalmos, and in the size of the goitre. Patients with old severe nervous changes showed practically no improvement. Among the 115 cases there were infrequent recurrences of the symptoms; these were again treated by the same methods with satisfactory results. The author considers that toxic goitre is caused by an hereditary or acquired alteration in the 'nervous net'; it is one of the nervous dystrophies with special changes in the thyroid gland and other organs.

Vitamin C—On the basis of a research on the influence of diets with excess and with deficiency of vitamins on the thyroid, C. Carrière *et al.* have treated with satisfactory results cases of toxic goitre by vitamin C in large doses and diets rich in that vitamin. The experimental research was carried out on rabbits, rats, and guinea-pigs. Vitamins A and C in large doses produce hypothyroidism, whereas diets deficient in these vitamins have the opposite effect. Large doses of vitamin D at first strongly stimulate thyroid activity, but the prolonged treatment is followed by degeneration of the thyroid and hyposecretion.

Surgical—M. Taffel and S. C. Harvey treated 52 cases of hyperthyroidism with a 2-stage operation, namely subtotal hemithyroidectomy followed 5 to 15 days later by subtotal extirpation of the remaining lobe. They found that this method was as successful as that in which the 2 operations were separated by an interval of 6 to 12 weeks. There were 39 females and 13 males in the series. The longer interval between the operations has the disadvantage that some patients do not return for the second operation, that the original level of hyperthyroidism may recur between the operations, and that the period of invalidism is much longer and places an increased economic strain upon the patient. To avoid wound infections due to the opening of the wound so soon after operation, the authors avoided prolonged drainage whenever possible, and used fine silk sutures with success.

C. W. Mayo and W. C. Simpson incorporated a sea sponge into the post-operative dressings in 82 of 179 thyroidectomy wounds. The sponge applied even elastic pressure to the area, thereby preventing serum from collecting under the skin, and lessening the period of drainage from an average of 10 to 9 days. In 112 cases in which the wound was closed without primary drainage, the period was reduced from 9 to 7 days, and 51 per cent of them had no drainage, as opposed to 40 per cent in the control group. The average period of drainage after the thyroidectomy for exophthalmic goitre was 5 days longer than that of adenomatous goitre. This difference was eliminated by the use of the sponge, which was found to have no effect on the development or duration of drainage after thyroidectomy for adenomatous goitre.

Of diarrhoea—R. May reported on the treatment of diarrhoea in toxic goitre. Digestive disturbances in these patients are usually very difficult to influence as most of them have a constant hypertonus, a highly-strung nervous system, and increased vasomotor action. It was thought that the vagus-stimulating action of acetylcholine might check these severe diarrhoeic attacks, and acetylcholine was tried on a number of patients. It was found that, though acetylcholine acted by stimulating the intestinal wall in other cases, in patients with toxic goitre it inhibited

increased peristalsis. The dose was 0.1 g. of acetylcholine intramuscularly over a few days.

- Adler, H. (1939) *Dtsch. med. Wschr.*, **65**, 909.
 Atkinson, F. R. B. (1938) *Brit. J. Child Dis.*, **35**, 268.
 Carrière, C., Morel, J., and Gineste, P. (1939) *Bull. Acad. Méd. Paris*, **121**, 324.
 Daniel, R. (1938) *Proc. Mayo Clin.*, **13**, 683.
 Ginsberg, E. (1939) *Viach. Dyelo*, **21**, 81.
 Lahey, F. H. (1931) *Ann. Surg.*, **93**, 1026.
 May, R. (1939) *Dtsch. med. Wschr.*, **65**, 1003.
 Mayo, C. W., and Simpson, W. C. (1939) *Proc. Mayo Clin.*, **14**, 316.
 Puppel, I. D., and Curtis, G. M. (1938) *Arch. Path.*, **25**, 1093.
 Sanchez-Calvo, R. (1939) *Endokrinologie*, **21**, 355.
 Scarlett, E. P. (1939) *Canad. med. Ass. J.*, **41**, 12.
 Taffel, M., and Harvey, S. C. (1939) *Ann. Surg.*, **109**, 437.
 Tiemann, F. (1939) *Dtsch. med. Wschr.*, **65**, 1067.
 Wilder, R. M. (1938) *Proc. Mayo Clin.*, **13**, 686.

Thyroiditis

Riedel's thyroiditis, although rare, is not so uncommon as is usually considered. Peculiarities of this condition are the iron-like hardness of the gland, with accompanying dysphagia, dyspnoea, and dysphonia. From the histological point of view there is alteration and atrophy of the epithelial elements, with fibrosis and almost complete lack of colloids. Radium has been used successfully in the treatment of Riedel's thyroiditis, and J. M. Renton *et al.* give 5 case reports in each of which the application of a radium collar resulted in freeing the patient from symptoms of dysphagia, dyspnoea, or dysphonia, and reduction of the swelling. From the clinical standpoint the similarity between Riedel's thyroiditis and malignant disease is marked, but the response obtained in Riedel's thyroiditis by the use of radium contrasts so favourably with the results obtained in malignant disease that its application may be regarded as a means of diagnosis. None of the cases treated with radium has shown any sign of thyroid deficiency, and there has been no sign of recurrence in periods ranging from 2 to 5 years. Patients received over the skin of the thyroid region at a distance of 3 cm. a dose of 2,500 r in 96 hours of continuous treatment.

Renton, J. M., Charteris, A. A., and Heggie, J. F. (1938) *Brit. J. Surg.*, **26**, 54.

Tumours

Adenomas

Treatment. H. R. G. Poate criticized the adjective 'simple' as applied to an adenoma which was always a potential source of grave danger to the patient. As regards toxicity, the dangerous age-periods were (i) from 30 to 35, when a relatively acute toxic condition might supervene, and (ii) from 45 to 50 when a low-grade toxicity of long standing might cause cardiac failure. The surgical removal of large adenomas was associated with the danger of the production of a "scabbard" trachea or absorption or weakening of cartilaginous rings, leading to post-operative tracheal collapse. As it was generally agreed that one per cent of adenomas ultimately became carcinomatous, the author advocated removal of any definitely palpable adenoma, irrespective of age. In thyroid disorders care must be taken to regulate the dosage of iodine to the needs of the individual. In disorders of secretion, i.e. in thyrotoxic states, iodine was usually given in large doses and often for prolonged periods. The author stated that the best results were obtained by small doses for short periods, and that usually it should be used only as a pre-operative measure, the patient being at rest in bed, because when once its beneficial effect was lost the patient could never regain his previously good condition. It was seldom advisable to give more than 3 drops of Lugol's solution 3 times a day, but in acute conditions 5 drops were sometimes given for a few days only with good results, and such treatment did not cause iodine thyroiditis, and so operation was easier than if there was a brittle gland which would not strip from the surrounding fascia.

Metastasizing Adenoma

Under the names of metastasizing and malignant adenoma, cases have been

recorded since 1876 in which there occurred metastases composed of thyroid tissue without any obvious primary carcinoma in the thyroid. These growths often occur in bone and notably in the skull. M. M. Cruickshank reported such a case in a female Hindu aged 55 years with a tumour about the size of a lime, involving the upper anterior aspect of the right frontal bone, and which was diagnosed as a meningioma. It pulsed, and a radiograph showed a large erosion in the position of the tumour. After removal in 2 stages the tumour was found microscopically to be 'a benign metastasizing struma'. Examination of the patient's thyroid was negative, and a further radiological examination of the skeleton showed nothing abnormal. Examination 4 months later, however, revealed a small nodular mass, of which the patient was quite unaware, about the size of a hazel nut in the right lobe of the thyroid. The patient refused operation.

Cruickshank, M. M. (1938) *Indian med. Gaz.*, **73**, 656.

Poate, H. R. G. (1938) *Med. J. Aust.*, **2**, 635.

GONORRHOEA

See also Vol. VI, p. 1, Cumulative Supplement, Key Nos. 575-578, and p. 155 of this volume.

Gonorrhoea in Males

Treatment

M & B 693, and mercuric oxycyanide irrigations.—From analysis of 65 cases E. L. Prebble found that M & B 693 definitely shortens the time necessary for the cure of acute gonorrhoea, and that it is more effective when combined with irrigation by mercuric oxycyanide solution. Some cases fail to respond and relapses are fairly common, but response to other forms of treatment following chemotherapy is satisfactory. Complications are very rare. The drug is much less toxic than sulphanilamide, it is slightly more toxic than uleron, but more certain in its action.

Local injection of glycerin. R. L. Raymond *et al.* point out that the antiseptic treatment of gonorrhoeal urethritis is very unsatisfactory, and that neither local irrigation nor oral therapy can affect organisms in the Littre gland. The authors have tried the osmotic effects of glycerin injected into the urethra, to wash out organisms from the deeper layer with the stream of bactericidal tissue fluids. Irrigation with potassium permanganate 1 in 8,000 is performed as a preliminary, and one grain of acriflavine is added to each 5 fluid ounces of glycerin to ensure that it is sterile. The glycerin is injected with a sterile syringe with a rubber olive on the nozzle, and is retained as long as the patient can conveniently tolerate it. The injection is given once a day, but twice is better. The treatment is essentially that of the anterior urethra, but, even so, benefit is derived when the posterior urethra is involved. The percentage of cases cured or relieved in the glycerin treated group and in the non-glycerin treated group is more or less the same, but the important feature is the reduction of the stay in hospital from an average of 33 days to an average of 18, i.e. a reduction of 45 per cent.

Prebble, E. L. (1938) *Lancet*, **2**, 1163.

Raymond, R. L., De, K. K., and Nyun, U. S. (1938) *Indian med. Gaz.*, **73**, 729.

Gonorrhoea in Adult Females

Diagnosis

Injection of ergotamine tartrate. E. Ramel and P. Berthoud recommended a test for facilitating the diagnosis of gonorrhoea of the female urogenital organs and of the rectum. Often gonorrhoea of women escapes attention because of the relative mildness of the infection. In these cases of blenorhagia the authors recommended the intramuscular injection of ergotamine tartrate (a constituent of neo-femergin), a sympatholytic drug. One c.cm. of the drug is injected, and 24 hours later swabs are taken from the rectum, urethra, vagina, and cervix. The absence of a gonorrhoeal infection should be diagnosed only if three consecutive tests are normal and free from gonococci. This method proved to be of very great value in the last 18 months, during which the authors used it in all cases of suspected blenorhagia. The same

test was applied about 3 weeks after the end of the treatment in order to find out by provocation if any latent gonococcal foci were left in the urogenital system.

Treatment

Sulphonamide drugs—F. L. Adair *et al.* discuss the use of sulphanilamide in the treatment of gonorrhoea in women. The drug has been found in the cervical secretion and menstrual fluid, but in amounts so small that its bactericidal action on the gonococcus is questioned. The assessment of cure for gonorrhoea should be based on cultures as well as smears. Sulphanilamide is excreted in breast milk both free and as the acetyl derivative. With doses of 30 and 60 grains, the total amount excreted was never greater than 1.5 per cent of the amount of the drug administered. It is transmitted to the placenta and foetus of the rabbit and is associated with a marked increase in the mortality of the young. Sulphanilamide has also been found in the placenta and in the blood of the umbilical cord of the human infant. The drug should be administered with the utmost caution during pregnancy and the period of lactation, and breast feeding should be discontinued while it is excreted in the milk.

I. Schaefer administered uleron and albucid to pregnant women suffering from gonorrhoea and to women suffering from inflammation of the adnexa. Five pregnant women were treated with 3 g. of uleron or albucid daily for 5 days. The treatment was repeated when necessary after an interval of 7 days, and douching with potassium permanganate solution was carried out. Two patients were free from gonococci after one treatment, one required 2 treatments, the fourth patient had an abortion which, however, was not necessarily due to the uleron, the fifth had 3 courses of treatment without success, but did not suffer from toxic effects. Of 6 patients with inflammation of the adnexa and parametritis, 5 were cured after 1 to 4 courses of treatment. In 2 inflammation of the adnexa was much improved (4 and 2 courses respectively) and in 3 was only slightly improved (3, 1, and 1 course respectively).

Tests of Cure

K. Sommer and H. Ruther state that it is difficult to determine when a woman with gonorrhoea is cured. In chronic gonorrhoea in females, diagnosis and prognosis are very difficult, and ascent of the gonococci must be prevented. After treatment with uleron a good many false cures have been observed, and the mistake often found too late to prevent ascent, and consequent sterility. The authors recommended making a bacteriological examination on the second day of the period, as then there is a great probability of finding gonococci (biological provocation). Microscopical examination must be accompanied by culture. The authors found a 96.5 per cent probability of making a correct diagnosis and prognosis if a culture is made, and a 74 per cent probability if microscopic examination only is made. Their scheme of examination was (i) after uleron treatment one microscopic examination daily for 10 to 12 days; (ii) on the second and seventh day one culture each, (iii) on the tenth day after provocative treatment, 5 or 6 microscopic examinations and one culture, (iv) culture on the second day of the period following the close of the treatment.

Adair, F. L., Hesseltine, H. C., and Hac, L. R. (1938) *J. Amer. med. Ass.*, **111**, 766.

Ramel, E., and Berthoud, P. (1939) *Schweiz. med. Wschr.*, **69**, 475.

Schaefer, I. (1939) *Dtsch. med. Wschr.*, **65**, 373.

Sommer, K., and Ruther, H. (1939) *Dtsch. med. Wschr.*, **65**, 90.

Gonorrhoea in Both Sexes

Complication

Liver damage—H. Wanek observed the development of liver damage in the course of gonorrhoea. Catarrhal jaundice is the form most frequently met with, but acute yellow atrophy may also occur. Liver damage, which was diagnosed after the usual tests, occurred in cases treated locally and in those treated with vaccine. It is most probably due to the action of the gonotoxins which act on the liver substance. Thirty per cent of the cases admitted to the author's ward showed liver damage on examination. Gonotoxic icterus should therefore be recognized, and, in all cases of gonorrhoea, function tests should be carried out in order to prevent further damage.

Diagnosis

P. Asch found a great many cases of gonorrhoea in which he could not find any

history of infection. He thinks that there are 'carriers' of gonococci without any clinical symptoms of gonorrhoea. There are chronic carriers who have a supposedly cured gonorrhoea. Very careful inspection and examination will always reveal pathological findings, either tiny abscesses in the urethra, or gonococci in the prostate after massage. There are also acute carriers who have been infected a short time (2 days to 2 months), but in whom no clinical symptoms have developed. If it is impossible to find gonococci in suspected carriers, a method of provocation should be used. He describes two types of atypical gonococci 'microgonococci' and 'macrogonococci'. The first are gonococci in the developmental stage, whilst the latter are gonococci in the dying-out stage. He describes the case of a man who was infected with macrogonococci from a woman who was free from gonorrhoeal symptoms. The atypical gonococci caused a gonorrhoeal urethritis in the man.

Treatment

Fever therapy.—C. A. Owens *et al.* investigated the results of treatment of gonorrhoea in various groups by sulphanilamide therapy, by fever therapy, and by a combination of the two forms of treatment. Although it had been thought that sulphanilamide would displace fever therapy, it was found that certain cases either did not respond to sulphanilamide or had an idiosyncrasy to the drug.

The authors suggest that every case of gonorrhoea should be given sulphanilamide in adequate dosage, but, if this fails, the alternatives include a single 10-hour session of fever therapy at 106–107 °F, for a combination of sulphanilamide and a single fever session at 106–107 °F (this will probably cure almost 100 per cent of cases). The possibility is that in the near future the use of sulphanilamide may allow a somewhat less prolonged session of fever therapy, possibly at a lower temperature. Artificial fever therapy is still considered by the authors to be the treatment of choice for gonorrhoeal complications.

In the experience of W. Bierman and C. L. Levenson fever therapy has proved an effective and rapid means of treating gonococcal infections. Briefly, their technique consists of the application of differential and intensive heating to the pelvic organs, combined with maintenance of the systemic temperature at, or below, 106.5 °F. A series of 165 cases is reviewed, 125 female and 40 male, 40 of these cases were gonococcal arthritides.

A photothermal cabinet, fitted with carbon-filament lamps, was used for elevating the systemic temperature, in conjunction with the short-wave current. Diathermy was used for the local heating. An average of 1 to 3 treatments was given, and in the arthritic group the average number was 2.69. Satisfactory results were obtained in the majority of cases, and follow-up studies showed that the results obtained were permanent. The authors emphasize that the cases treated had failed to respond to any other form of treatment.

Sulphonamide drugs. In an attempt to assess fairly the claims made in numerous publications on behalf of the action of uleron in gonorrhoea, C. Hamilton Wilkie used it in 2 groups of cases: (i) 100 patients treated at an early stage, and (ii) 20 patients, resistant to older methods of treatment, given uleron at a late stage of infection. The drug was administered in short 3-day courses separated by varying short intervals (usually 9 days) and was combined with daily irrigations of potassium permanganate. The scheme of dosage was: on the first day 2 tablets 3 times a day after food and on the second and third days 2 tablets 4 times a day. The quantity employed in a 3-day course was 22 tablets (11 g.). In group (i) there were 74 per cent of cures, 17 per cent of failures, and 9 per cent of relapses. In group (ii) there were 5 failures in 20 cases. Polyneuritis was not observed; a general urticaria appeared in 2 cases but cleared up one week after cessation of the drug.

H. O. Loos employed, in 43 males and 17 females with gonorrhoea, albucid (*para-aminobenzenesulphonacetamide*) which is easily absorbed by the intestinal mucous membrane, excreted after 3 to 4 days through the kidneys, and not very toxic (in animal experiments). The author gave a course of 2 tablets each of 0.5 g. thrice daily for 3 days (9 g.); this was followed by an interval of 5 to 7 days, then a second course and, if necessary (rarely), a third course. After treatment there was an observation period of 10 days. Of 60 patients, 49 were completely cured after an average of 28 days with an average dose of 15.5 g., 22 patients were treated with 1 course, 31 with 2, and 7 with 3. All the cured cases were cured after the second course, no third course of treatment being necessary.

Asch, P. (1938) *Schweiz. med. Wschr.*, **68**, 934.

Bierman, W., and Levenson, C. L. (1939) *Radiology*, **32**, 454.

- Loos, H. O. (1939) *Derm. Wschr.*, **108**, 509.
 Owens, C. A., Wright, W. D., and Lewis, M. D. (1938) *J. Urol.*, **40**, 847.
 Wanick, H. (1939) *Med. Klinik*, **35**, 639.
 Wilkie, C. H. (1939) *Brit. med. J.*, **1**, 57.

Vulvo-Vaginitis in Children

Treatment

C. McK. Burpee *et al.* studied the relative merits of the following three types of treatment in 112 cases of gonorrhoeal vaginitis. (i) Intramuscular injections of theelin (oestrone) in oil were given to 47 patients, 41 of them or 87 per cent were cured but 5 relapsed. Five patients treated with theelin and the vaginal application of 1 per cent silver nitrate jelly were cured, and there were no recurrences. (ii) Fever was produced in another group of patients by the intravenous injection of typhoid vaccine, and in 5 patients with the Kettering hypertherm. Apparent cures were obtained in 8 out of 19 cases, or 42 per cent, and there was one recurrence. (iii) Sulphanilamide given orally produced apparent cure in 11 out of 22 cases. There was one recurrence. Two patients were cured by combined treatment with fever and sulphanilamide and there was one recurrence. In this series, therefore, the final results obtained with theelin were better than those obtained with the other methods. When relapses occurred in the theelin treatment the authors attributed them to reinfection from foci within the urethra or rectum. There are possible dangers in this procedure, namely, (i) development of secondary sexual characters, (ii) a deleterious effect on the ovary, and (iii) changes in the upper genital tract, aiding the spread of gonococcal infection to the tubes and ovaries. In a few of the cases, enlargement of the breasts and growth of pubic hair was noticed, but these disappeared on the cessation of treatment. One case developed gonococcal salpingitis during a course, but it was impossible to assess whether the action of the theelin had helped to infect the Fallopian tubes.

Oestrogens.—K. Herrnberger examined the vaginal epithelium in 62 children of various ages before and after treatment by follicular hormone with doses varying between 100 and 10,000 I.B.U. of oestradiol benzoate and given once or several times. 1,000 I.B.U. proved to be a minimal dose for the full transformation of the infantile vaginal mucous membrane into the adult form. A single dose of 10,000 I.B.U. in oil given intramuscularly was sufficient to promote full development to the adult type of mucosa. The vagina remained in an adult state if further doses of 1,000 I.B.U. were given daily by mouth. The optimal dosage is 1,000 I.B.U. of alcoholic solution given by mouth for about 17 days.

C. Mazer and F. R. Schechter treated vulvo-vaginitis in children with oestrogen. The disease is often due to the gonococcus, but other organisms appear, and they produce the inflammation because the resistance of the vagina and its secretions to invasion has been lowered. With the use of vaginal suppositories of oestrogen, 33 of 34 children were cured, and there were no recurrences. Three children were given oestrogen by mouth, but it was found to be ineffective. It was found necessary to continue the treatment for 8 weeks, in spite of evidence of cure, in order to guard against recurrences.

Burpee, C. McK., Robinow, M., and Leslie, J. T. (1939) *Amer. J. Dis. Child.*, **57**, 1.

Herrnberger, K. (1938) *Dtsch. med. Wschr.*, **64**, 1873.

Mazer, C., and Schechter, F. R. (1939) *J. Amer. med. Ass.*, **112**, 1925.

GOUT

See also Vol. VI, p. 37, and Cumulative Supplement, Key No. 579.

Aetiology

After Salyrgan

Five cases of congestive cardiac failure in which attacks of gout followed the intramuscular injection of 1 c.cm. of salyrgan (mersalyl) every second day are described by N. Lloyd Price. Ammonium chloride, in doses of 20 gr. 3 times a day by mouth, had also been given, and the fluid intake was restricted. All the patients had had previous attacks of gout, which were always immediately preceded by a 'critical'

diuresis occurring 7 to 9 days after the commencement of salyrgan therapy. The occurrence of gout in patients receiving salyrgan is of bad prognostic significance as they usually succumb within a few weeks of the attack. The attacks of gout are due to the diuresis rather than to the level of the uric acid in the blood or oedema fluid, and it is suggested that the associated disturbance of electrolyte balance due to salyrgan is important in causation.

Price, N. L. (1939) *Lancet*, **1**, 22.

Treatment

Diet

E. C. Bartels tried to show that chronic gout could be controlled by a diet rich in carbohydrates and low in fats and purins. In addition, cinchophen was given periodically to increase the uric acid excretion in the urine. The dosage was $7\frac{1}{2}$ gr 3 times a day, for 3 days each week. At the beginning of treatment meat, fish, or fowl was given at one meal only on 2 or 3 days a week, later it was given more frequently if the uric acid level allowed. Uric acid determinations of the whole blood were made, the normal being below 4.5 mg. per cent, and of the serum, the normal for which is 6 mg. per cent. The author claimed that the good results obtained seem to warrant further investigation.

Bartels, E. C. (1939) *New Engl. J. Med.*, **220**, 583.

HAEMATEMESIS

See also Vol. VI, p. 75, and p. 47 of this volume.

Aetiology

A. T. M. Wilson investigated 50 patients with severe haematemesis, and found that in practically every case the haematemeses were preceded by intense emotional stress, most often related to their work, financial matters, or illnesses of near relatives.

Wilson, A. T. M. (1938) *J. ment. Sci.*, **84**, 1087.

Prognosis

S. Hesser states that, in 122 cases of relapsing gastric haemorrhage, he found that relapse often occurs in bleeding gastric ulcers, and that 30 per cent of all haemorrhages are bleeding gastric ulcers. In about half of the cases, relapse occurred only once, but it may occur very often. Relapses occur more often in men than in women. The average age of his patients was between 30 and 60 years. There were about twice as many duodenal ulcers as gastric ulcers in his cases. The mortality in this series was 3.3 per cent (4 cases) whilst the figure for primary haemorrhage was 3.9 per cent. Operations on the stomach for peptic ulcer did not prevent relapse of bleeding, as the 30 operated cases of the author show. The author considers therefore that previous haemorrhage should not be regarded as an indication for operative measures.

Hesser, S. (1939) *Acta med. scand.*, **98**, 340.

Treatment

Drip Blood-Transfusion

Fifty cases of haematemesis and melaena, due to gastric and duodenal ulceration and treated in the medical unit at St. Bartholomew's Hospital, were described by F. Avery Jones. In 13, the haemorrhage recurred and in 10 there were 3 or more haematemeses. The only death occurred in a woman 69 years old with erosive gastritis. This contrasted with another series of 21 cases in which more than one attack of haematemesis occurred at the same hospital (Cullinan and Price, 1932); 12 deaths occurred. Patients were treated on the lines inaugurated by Witts and were allowed semi-solids from the first and an average daily fluid intake of 2,700 c.cm. The drip blood-transfusion method of Marriott and Kekwick was used, (i) when severe general shock was indicated by a systolic blood pressure below 90 mm. Hg and a pulse-rate above 120, and (ii) when the percentage of haemoglobin fell

below 40. If symptoms did not suggest continuous bleeding, 600 to 1,200 c.cm. of blood were given. When continuous bleeding was present the drip was maintained until all signs of haemorrhage had ceased and until up to 3,000 c.cm. had been given. The drip method may take from 3 to 6 hours, in contrast to the normal transfusion time of 15 to 30 minutes. After the average haematemesis the systolic blood-pressure was normal or slightly raised, and the highest sphygmomanometer readings were found from 6 to 24 hours later. The drip method did not stimulate further haemorrhage; in most cases bleeding ultimately stopped under this treatment, though in others it might be necessary to persevere and to give several transfusions. In 3 cases it was necessary to give more than 6,000 c.cm. of blood.

Jones, F. A. (1939) *Brit. med. J.*, **1**, 915.

HAEMATOPORPHYRINURIA

See also Vol. VI, p. 85

Aetiology

J. T. Brygsh pointed out that various pathological conditions of the liver disturb metabolism of blood pigment and that an increase in the formation and excretion of porphyrin occurs as a result of poisoning by lead, neoarsphenamine, cinchophen, and thiosinamine. The author has found that alcoholic excess, by acting on the cells of the liver, bone marrow, and reticulo-endothelial system, causes increased porphyrinuria.

Brygsh, J. T. (1937) *Proc. Mayo Clin.*, **12**, 609.

HAEMATURIA

See also Vol. VI, p. 97.

Treatment

Vitamin C

The administration of vitamin C was carried out with successful results by C. I. Burkland in 4 cases of essential haematuria. Essential haematuria is a result of increased permeability of the capillaries, which in turn is due to some fault in the intercellular cement material of the capillary endothelium. One of the main functions of vitamin C is the regulation of the formation of this cement substance. Treatment consisted of a high vitamin C diet, supplemented by ascorbic tablets orally, and large doses of the sodium salt of ascorbic acid by the intravenous route. An additional action of vitamin C is that of increasing the coagulability of the blood combined with the stimulation of adrenaline secretion and its role as a catalyst of cellular metabolism.

Burkland, C. F. (1939) *J. Urol.*, **41**, 401.

HAEMOPHILIA

See also Vol. VI, p. 123

Aetiology

In the Wesley M. Carpenter Lecture on haemophilia W. H. Howell confirmed the statement of W. Bulloch and P. Fildes that an authentic female bleeder has not been recorded, although theoretically, if a male haemophilic married a female conductor he might have a haemophilic daughter as well as a haemophilic son. On the vexed question of the *de novo* origin of sporadic cases without any history of heredity, the view was suggested that such an event is a true hereditary condition which has arisen *de novo* by a mutation of the sex cells of the mother. The real difference between haemophilic and normal blood was that haemophilic blood contained less thromboplastin in its plasma. With regard to treatment, Howell has found that the tissue extract, made with glycerin, of dried lung was unusually potent, and retained its activity for a long time if kept in the ice box. The hypothesis that the haemophilic was wanting in the female sex hormone (Burch) was tested, but there was not any positive effect from injections of theelin, upon the coagulation time of haemophilic blood.

Treatment

Howell had tested but also without effect the following suggested remedies. nateina tablets, Llopis, a mixture of vitamins, A, B, C, D, with calcium phosphate and sugar, ceanothyn, the mixed alkaloids of *Ceanothus americanus*; cephalin, a crude extract of brain in aqueous suspension, a liver and grape-fruit diet, spleen and bone marrow, ovarian, placental, dried lung extracts, cod-liver oil, brewers' yeast, rivanol, hexylresorcinol, carbon tetrachloride, sodium bicarbonate and alkalis, ammonium chloride acidosis, fasting for 48 hours, and solution of purified thromboplastin, obtained from lung, by the mouth. At present the control of haemophilia must be based chiefly on transfusions, but there is a prospect that further study of the chemistry and reactions of thromboplastin might provide a more convenient treatment in which the dosage might be regulated to meet the severity of the symptoms

Ovarian Extract

A. Kocsis and A. Hasskó arguing that, although women transmit haemophilia they are not bleeders, postulated that there must be some inhibitory mechanism in the female which prevents bleeding. They thought that this inhibition might be caused by ovarian hormones and tried these on several patients. In an 11 years' old boy from a haemophilic family (with 16 deaths from haemophilia), when a severe bleeding occurred it was stopped after 3 days by injection of 40 c cm. of paternal blood and 1 c cm. of ovarian extract (given for 9 days). Another case was that of a man, 34 years old, who had to have a tooth extraction and was treated beforehand with perioral ovarian extract (10,000 mouse units of hogival) for 4 days, for a further 2 days with injections of 2 c cm. of an ovarian extract, glanduovin (corresponding to 5 g. ovarian tissue) and 3 days later with one injection of 10,000 mouse units of the follicular hormone glandubolin. After a further injection of colutoid (extracts of corpus luteum, pineal, pituitary, and thymus) 2 teeth were extracted with very little bleeding.

Bullock, W., and Fildes, P. (1911) *Treasury of Human Inheritance*, pt. 5-6, Sect. 14a

Burch, C. L. (1931) *J. Amer. med. Ass.*, **97**, 244

Howell, W. H. (1939) *Bull. N.Y. Acad. Med.*, 2nd ser., **15**, 3.

Kocsis, A., and Hasskó, A. (1938) *Dtsch. med. Wschr.*, **64**, 1284

HAEMOPTYSIS

See also Vol. VI, p. 130, and Cumulative Supplement, Key No. 595.

Treatment

Oxygen Injection

R. Molari reported on the treatment of tuberculous haemoptysis by the subcutaneous injection of 300 to 400 c cm. of oxygen. Out of 26 cases, 21 reacted favourably to the treatment, haemoptysis stopped within 10 minutes of the injection. In the author's opinion, the oxygen seemed to cause hypotension which lasted about 10 hours, and the basis of which was the vasodilatation produced in the arterioles of the subcutaneous tissue. In a few cases side-effects, such as slight nausea and general discomfort, occurred, but the haemoptysis stopped within a few minutes of the injection. The author concluded by reviewing the extensive French and Italian literature on this subject.

Molari, R. (1939) *Riv. Pat. Clin. Tuberc.*, **13**, 218.

HAEMORRHAGIC DISEASES

See also Vol. VI, p. 138.

Thrombocytopenic Purpura

N. Rosenthal studied 153 cases of thrombocytopenic purpura. Blood examination of these patients showed: (i) no anaemia unless much haemorrhage had occurred, (ii) a normal leucocyte picture, and (iii) a marked reduction in the number of

platelets. Bruising, purpura, epistaxis, and other signs of bleeding were present in all cases. Twenty-nine per cent of the cases occurred in the first decade of life. From 10 to 40, the average incidence was about 17 per cent, and after that it decreased. The acute forms are more common in children and the chronic forms in adults. Spontaneous recovery for periods varying from 2 weeks to 7 months occurred in some of the cases up to the age of 20. Most of the cases were idiopathic, but 12 were associated with infection and 16 with drug idiosyncrasy. Food allergy was not an aetiological factor in this group, and Rosenthal stated that cases associated with neoplasm involving the bone marrow are not common. The acute cases were divided into 3 groups, (i) those who spontaneously recovered (38 per cent), (ii) those who became chronic, and (iii) cases of the markedly acute type in whom the disease rapidly terminated fatally. Splenectomy had no effect on these cases. In the chronic cases, some were mild and some more severe. Three of them were recurrent in type. Splenectomy benefited, and resulted in cure in most chronic cases. The use of snake venom resulted in improvement in 50 per cent of cases of chronic purpura; blood transfusion is of value in severe cases, while among the acute varieties ascorbic acid and liver extract have considerable effect.

Pathogenesis and Morbid Anatomy

C. I. Troland and F. C. Lee extracted with acetone from the spleen of patients suffering from idiopathic thrombocytopenic purpura a factor which would reduce the number of circulating platelets in rabbits. After the reduction there was a sharp rise, and then a return to normal. This suggests that the factor is destroyed or excreted by the animal. In no case did it produce purpura. It was given intravenously and termed thrombocytopen by the authors. Boiling decreased its effect. The concentration of thrombocytopen in different spleens varied, and it was suggested that in some cases it may also be present in other organs or in the reticulo-endothelial system, thereby diminishing the amount in the spleen. Control experiments with normal splenic tissue showed that it did not contain thrombocytopen.

Rosenthal, N. (1939) *J. Amer. med. Ass.*, **112**, 101.

Troland, C. I., and Lee, F. C. (1938) *J. Amer. med. Ass.*, **111**, 221.

HAIR FOLLICLES. ABNORMALITIES AND DISEASES

See also Vol. VI, p. 162

Lanugo Hair

A. Castellani drew attention to some fairly common and little-known conditions of the lanugo hair. Hypertrichosis of the hair of the limbs had been seen in malnutrition, in hot summer weather, and in one case in the winter. Patches of alopecia of the lanugo hair have been found on various parts of the body, most frequently the legs, and might occur in conjunction with alopecia areata of the scalp. A symmetrical alopecia, unassociated with any general or local inflammatory lesion, was fairly common on the lower extremities and sometimes on the arms.

Castellani, A. (1938) *J. trop. Med. (Hyg.)*, **41**, 400.

HEADACHE

See also Vol. VI, p. 199, and Cumulative Supplement, Key No. 618

Types of Headache

Erythromelalgia of the Head

B. T. Horton *et al.* described a type of vascular headache which they termed 'erythromelalgia of the head'. It was associated with vasodilatation, and characterized by recurrent attacks of boring pain in the eye, temple, neck, and sometimes the face on one side. These headaches were nocturnal and might last from 15 minutes to several hours. There is sometimes nausea but no vomiting, and scotomas are absent. Other signs of vasodilatation on the affected side are also present such as flushing of the face, a rise of skin temperature, and watering and injection of the conjunctivae. The headache can be relieved by pressure on the appropriate carotid artery, and can be induced in susceptible cases by the subcutaneous injection of

0.3 to 0.5 mg. of histamine. The authors treated 84 cases of this type of headache with 0.05 mg. of histamine subcutaneously twice daily for 2 consecutive days and 0.066 mg. twice daily for the next 2 days. On the fifth day 0.1 mg. was given twice and was continued at the same rate for 2 to 3 weeks. Sixty-five of the patients were free from headaches for periods varying from 2 weeks to 18 months while 19 received no relief thereby.

Inflammation of Mucosa of Middle Turbinate

W. G. Mussun described a type of neuralgic headache accompanying inflammation of the anterior third or half of the mucosa of the middle turbinate. He has seen 26 to 28 patients with this condition, all adults and most of them past middle life. The pain usually began mildly and gradually became more severe with the passage of years. The pain was localized to the nasal side of the orbit, often involving the frontal region, and occurring on the same side as the inflamed turbinate, but in one instance involving the opposite side. It is intermittent and is uninfluenced by any condition save sleep. Many patients were awakened by the pain and others complained that it was worse on waking in the morning. The mucosa of the turbinate showed no morbid condition except inflammation, for which no cause could be found. It is necessary to diagnose the pain from such conditions as nasopharynx or supra-orbital neuralgia, and frontal sinusitis. Anaesthetizing the affected turbinate with cocaine may give relief which lasts for a long period. If the pain recurs, removal of adjacent structures pressing on the turbinate (usually the septum) followed by anaesthetization of the inflamed turbinate may bring about a cure. Should this fail amputation of the anterior end of the inflamed part of the turbinate results in permanent relief.

Horton, B. T., MacLean, A. R., and Craig, W. McK. (1939) *Proc Mayo Clin.*, **14**, 257.

Mussun, W. G. (1939) *Arch. Otolaryng., Chicago*, **29**, 39.

HEART DISEASES: CONGENITAL DISEASES

See also Vol. VI, p. 206

Patent Ductus Arteriosus

In an experimental radiological technique by A. I. Barclay *et al.* on full-term foetuses obtained by Caesarean section from ewes, thorotrast was at once injected intravenously, and the direct method of X-ray cinematography of the region of the ductus arteriosus employed. It appeared that the ductus arteriosus becomes functionally closed within one minute from the delivery of the foetus. This closure was due to the independent and intermittent activity of groups of muscular fibres leading to twisting and kinking of the vessel, and not to a rapid and simultaneous contraction of the total musculature of the ductus arteriosus. The appearances seen *in vivo* were very different from those found at necropsy.

Barclay, A. I., Barcroft, J., Barron, D. H., and Franklin, K. J. (1938) *Brit. J. Radiol.*, N.S. **9**, 570.

Fallot's Tetralogy

Clinical Picture

I. F. Volini and N. Flaxman reported a case of Fallot's tetralogy occurring in a man of 41 who died of uraemia due to chronic glomerulo-nephritis. The age to which the patient had lived was remarkable and only one case of Fallot's tetralogy which survived longer is recorded in the literature. The tetralogy consists of inter-ventricular septal defect, pulmonary stenosis and insufficiency, dextroposition of the aorta, and hypertrophy of the right ventricle. Clinically the case reported showed cyanosis, clubbing of the fingers, and oedema. The heart was enlarged downwards, to the left, and to the right. The pulse-rate was 56 and was regular and the blood pressure varied between 168 mm. systolic and 100 mm. diastolic. A systolic precordial thrill was present and a loud systolic murmur was heard all over the precordium and was conducted up into the neck. A diastolic murmur with maximal intensity at the sternal margin in the third left intercostal space was heard. In the aortic and pulmonary areas the systolic murmur was louder than the diastolic. The liver was

palpable below the right costal margin. The skin of the lower half of the legs was pigmented and scaly. The electrocardiogram showed right axis deviation and evidence of abnormal conduction in the bundle of His. X-ray examination showed enormous cardiac enlargement. At necropsy a typical Fallot's tetralogy was present in the heart.

Volini, I. F., and Flaxman, N. (1938) *J. Amer. med. Ass.*, **111**, 2000.

Cardiac Pentad

Clinical Picture

W. M. Feldman and S. G. Snook reported a cardiac malformation probably unique congenital cardiac pentad—Fallot's so-called tetralogy together with an interauricular septal defect. The lumen of the pulmonary artery admitted a fine probe at its orifice, but widened to a diameter of $\frac{1}{4}$ inch further along its course, and the ductus arteriosus was patent. There was a free communication between all the chambers of the heart which was thus a bilocular organ. The infant, a female aged 2 months, had been free from severe cyanosis for the first 6 weeks of life, then attacks of dyspnoea and cyanosis began to occur. It was suggested that the incompleteness of the 2 septal defects might explain the baby's almost normal colour between the asphyxial attacks. A plea is put forward for the substitution of the word 'tetrad' for 'tetralogy' which is rightly applied to a series of 4 related literary works.

Feldman, W. M., and Snook, S. G. (1938) *Brit. J. Child Dis.*, **35**, 183.

HEART DISEASES: RHEUMATIC HEART DISEASE IN CHILDREN

See also Vol. VI, p. 234

Aetiology

From experimental research and a review of existing knowledge, W. Pagel concluded that rheumatic nodules, in common with the epithelioid-celled tubercle elicited by an allergic tissue reaction should be regarded as allergic granulomas. The tubercle bacillus might also act as an antigen causing rheumatic manifestations as in some forms of erythema nodosum, but there was not any evidence that the tubercle bacillus was the common or a frequent causal agent of rheumatism, which was described as a clinical syndrome due to any toxic or infective agency. Aschoff's bodies have been described in Japan (Masugi, M., Murasawa, S., and Ya-Shu) in the heart of tuberculous patients, but Pagel had examined more than 200 such hearts and hardly ever found them, he therefore suggested that they are due to a special regional character of tuberculosis.

Masugi, M., Murasawa, S., and Ya-Shu (1937) *Yenchow Arch.*, **299**, 426.

Pagel, W. (1939) *Papworth Research Bull.*, **1**, 95.

HEART DISEASES: PERICARDIUM DISEASES

See also Vol. VI, p. 256.

Chronic Constrictive Pericarditis (Pick's Disease)

Clinical Picture

Kymography.—G. L. S. Konstam and F. G. Wood reported 2 cases of chronic constrictive pericarditis (Pick's disease) in which, among other methods of investigation, a careful kymographic study had been made. In one case a kymogram taken before operation showed that pulsations were almost absent along the right border of the heart, and not clearly defined along the left. Abnormal movements were seen in the middle arc region and in the upper ventricular region. The apex of the left ventricle was encased in calcium and was immovable. After operation, which consisted of trans-sternal pericardiectomy, there were increased pulsations along the left border, and at the apex of the left ventricle where they had previously been absent. An abnormal ventricular wave-form was present and was thought to be due to

unequal decompression. In the second case a kymogram was taken but, owing to the presence of dyspnoea, had to be taken during quiet respiration; it showed the heart moving to the right during expiration and to the left during inspiration. Normal pulsations were absent, except for slight movement at the apex of the left ventricle. This case was due to tuberculosis, and ultimately proved fatal.

Treatment

Surgical.—G. F. Strong described a case of Pick's disease occurring in a boy aged 19 years. The cause of the pericarditis in this case was unknown, and, in spite of frequent paracentesis and treatment with diuretics over many months, the patient continued to suffer from ascites and oedema. Pleural paracentesis was also necessary. At operation the adhesions between the pericardium and the heart, which were particularly dense over the auricles, were separated. Though standing the operation well, the patient still needed restricted fluids, and diuretics to keep his oedema down. Four months after the operation he suddenly noticed an increase in urinary output. No further diuretics were necessary and, apart from slight oedema of the legs at the end of the day, his oedema and ascites vanished. He was not entirely cured, as some dyspnoea still remained. Strong considered that, if it had been possible to still further remove the dense adhesions from the thin auricles, the operation would have been even more successful.

Pericardiectomy.—J. B Hunter and T. East deal with the surgical treatment of constrictive pericarditis and report 3 cases in which pericardiectomy was performed. All the patients were given considerable periods of rest in bed before operation. Ascites was controlled either by salyrgan (merisallyl) or by tapping, and as much fluid as possible was removed before operation. As an anaesthetic, plain open ether, preceded by morphine, was the most satisfactory. A curved incision was made, starting in the middle line of the sternum about one inch below the sternal notch, and carried outwards across the left nipple, sweeping back to end just across the middle line at the xiphisternum. The skin-flap thus marked out was turned to the right (see Fig. 14). Portions of the second to the sixth costal cartilages were carefully removed after the perichondrium had been stripped. A sternum-splitting chisel was introduced at the right border of the xiphisternum, and the sternum divided as far as the second interspace; a cross division was then made to the middle line from the second interspace. The sternal flap thus marked out was turned to the left as an osteoplastic

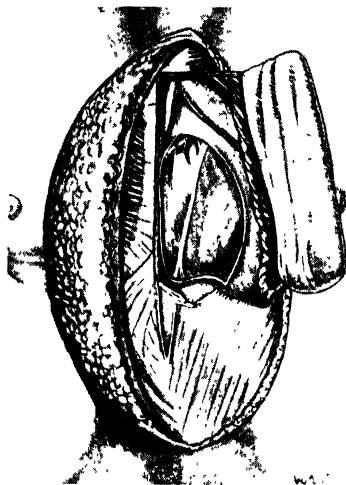
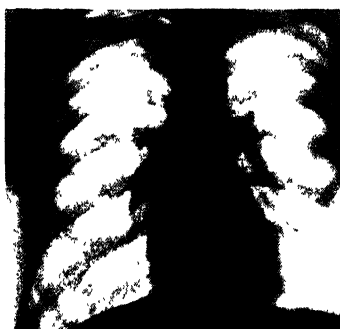


FIG. 14.—Technique of pericardiectomy: heart exposed, with skin-flap turned to right and osteoplastic flap (sternum) to left, showing fibrous band (found in case 2) running from right auricle, across right ventricle, to diaphragm (From *Lancet*, 1939)

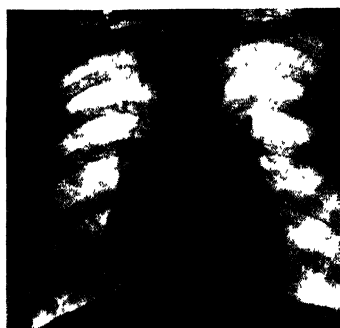
flap, giving a wide exposure of the pericardium and the edges of the pleurae. The pleurae were stripped back from the pericardium by gauze dissection. In all cases, there were fine extrapericardial adhesions which had to be separated far round to the left side before opening the pericardium. After free exposure of the pericardium, an incision was made into it with great care and a line of cleavage sought. When a portion had been freed, that portion was removed and a fresh portion separated, the pericardium being removed piecemeal. This removal was carried out over the anterior and left side as far on the right as possible and in an upward direction. No special attempt was made to free the superior and inferior venae cavae. In all cases a definite increase could be seen in the force of the heart beat, and the heart at the end of the operation was apparently larger. Cases 1 and 2 had developed chronic constrictive pericarditis (Pick's syndrome) about a year after acute pericarditis. Case 3 showed on radiography calcification in the pericardial sac although the syndrome had not developed (see Plate II). All 3 patients had pleurisy



A



B



C

Chronic Constrictive Pericarditis. Radiographs of Case 3, showing A, normal appearance of sternum and small granular calcifications in pericardial sac, B, size of heart before operation and C, increased size of heart after operation (From *The Lancet*, 1939)

PLATE II

with effusion after operation. Case 1 experienced apparent cure; in Case 2 there was some measure of relief; Case 3, in which the syndrome had not developed, showed improvement.

Partial pericardiectomy.—H. J. Stewart and G. J. Heuer treated 7 cases by partial pericardiectomy. Three of the patients were cured, 3 greatly improved, and the seventh is now convalescent after operation. Since the embarrassment to the circulation can only be relieved by resection of the obstructing pericardium, and in view of the good results obtained in their cases, the authors recommend that surgical treatment should be undertaken for this condition in favourable cases.

Hunter, J. B., and East, T. (1939) *Lancet*, **1**, 255.

Konstam, G. L. S., and Wood, F. G. (1939) *Brit. med. J.*, **1**, 498.

Stewart, H. J., and Heuer, G. J. (1939) *Arch. intern. Med.*, **63**, 504.

Strong, G. F. (1938) *Canad. med. Ass. J.*, **39**, 247

HEART DISEASES: MYOCARDIUM DISEASES

See also Vol VI, p. 277.

Acute Myocardial Infarction

C. K. Friedberg and H. Horn observed 34 cases of acute myocardial infarction without coronary thrombosis among 2,000 necropsies in 4 years. Of these, 6 were encountered in the first 1,000, and 28 in the second 1,000, the latter also including 63 cases of myocardial infarction due to coronary thrombosis. Three cases without thrombosis from a previous series were also included. In 32 out of 37 cases, severe myocardial degeneration was observed macroscopically, and in the remaining 5 microscopical evidence was provided by a study of recurrent pulmonary embolism. Of these 12 were associated with recent embolism, 8 were examples of calcified aortic stenosis, 6 were due to old coronary occlusion or cardiac failure, 4 were post-operative, 3 were caused by severe acute anaemia, 3 were due to malignant hypertension, and one to superior mesenteric occlusion. The myocardial lesions were caused by an intense ischaemia due to an impaired coronary blood supply. Apart from narrowing of the lumen of the coronary artery, the associated conditions such as pulmonary embolism or aortic stenosis act as contributory causes. In the latter, sudden death may be caused by severe ischaemia and necrosis without coronary thrombosis.

Friedberg, C. K., and Horn, H. (1939) *J. Amer. med. Ass.*, **112**, 1675.

Tumours of Heart

Stuart McDonald, Jnr., and J. C. Heather reported 2 cases of invasion of the pulmonary veins and the left auricle by malignant disease in males, aged 23 and 52 years, with pulmonary metastases due to myeloid reticulo-sarcoma of the lower extremity in the younger patient and a primary bronchial carcinoma in the older patient. The previously recorded cases were reviewed.

McDonald, S., Jnr., and Heather, J. C. (1939) *J. Path. Bact.*, **48**, 583.

Treatment

Foetal-Heart Hormone

B. Purjesz and A. Tószoghy reported their results with a foetal-heart hormone in the treatment of cardiac diseases. Miko and Toro found a foetal-heart hormone derived from hearts before the development of nervous elements. By means of various experiments the authors were able to prove that the action of the heart is not due to nervous elements, or to adrenaline-acetylcholine, but to this hormone, called by them 'corhormon'. This hormone acts on the nuclei of the heart muscle and stimulates mitosis, by which means regeneration takes place in the cardiac muscle. The authors examined the action of 'corhormon' on patients suffering from degeneration of the myocardium, angina pectoris, and, in one case, paroxysmal tachycardia. They found that the subjective phenomena accompanying myocardial disease suddenly disappeared and that the hormone was useful in hearts which were attacked by diphtheritic toxin. The hormone cannot build up muscle tissue from absolutely degenerated fibres, but it can encourage mitosis, and therefore regeneration of still

viable muscle. The authors were convinced that the hormone provides a real advance in the therapy of cardiac diseases and advocated its further trial. The doses given were 2 to 4 c cm. over 3 to 4 weeks, intramuscularly or subcutaneously.

Purjesz, B., and Tószoghy, A. (1939) *Schweiz. med. Wschr.*, **69**, 523

Stab Wounds of the Heart

Treatment

Surgical.—I. A. Bigger operated on 17 patients with heart wounds, 6 of whom died. When admitted with symptoms suggesting a cardiac wound the patient was placed in a moderate Trendelenburg position, given morphine and atropine and, if in a state of profound collapse, 5 minims of adrenaline solution hypodermically. The blood pressure was taken frequently, the general appearance noted, and the superficial cervical veins inspected. The thorax was examined for pneumothorax and haemothorax, and the heart percussed and auscultated.

The cases were divided into 4 groups and examples of each were cited: (i) Patients with a free communication between the pericardium and the pleura but only slight or moderate intrapleural haemorrhage were treated conservatively. (ii) Those with tamponade (compression of the heart by the haemopericardium) but in whom a marked improvement followed treatment with intravenous fluids, adrenaline, atropine, and morphine, they were prepared for operation, before which a cannula was inserted into the pericardium, the intra-pericardial pressure recorded, and if possible sufficient blood removed to lower the pressure appreciably. The cannula was then left in position to detect any rapid recurrence of tamponade, if so operation was performed, but if the pressure remained low, conservative treatment was continued. (iii) Those with increased intrapericardial pressure who do not respond to conservative treatment and in whom the arterial pressure remained low. They should be operated on immediately. (iv) Those with a free communication between the pericardium and the pleura containing a massive intrapleural haemorrhage. Few members of this group survived long enough to be treated by operation, which might be performed under local or general anaesthesia. Five of the patients were operated on under local anaesthesia. The lateral incision was preferable to the mid-sternal approach, and it was advisable to avoid an open pneumothorax, but this was often impossible. The recovery rate of penetrating heart wounds not operated on was about 10 per cent, whereas in those submitted to surgical treatment the chance of recovery was now about 50 per cent. The follow-up of 7 out of the 17 cases showed that the cardiac condition was excellent, and this agreed with the opinion of observers that, if the patient recovered, little or no permanent physical impairment resulted.

Bigger, I. A. (1939) *J. thorac. Surg.*, **8**, 239

HEART DISEASES: ENDOCARDITIS, MALIGNANT

See also Vol. VI, p. 297.

Subacute Bacterial Endocarditis

Prognosis

Subacute bacterial endocarditis due to *Streptococcus viridans*, became more frequent during and after the war, and is now less frequent. Thus in an analysis of 129 bacteriologically proved cases in the 26 years 1910-1937 the cases reached the peak in 1923 and fell since. J. A. Capps, who collected these cases, found that 11 of the patients were alive 5 years after the onset of the infection. In these cases the fever was less and embolic phenomena were less in evidence, no examples of cerebral embolism or Osler's nodes were noted. In contrast to the severe septic cases, the patients who recovered were not very ill and were mainly ambulant. The chief stress in treatment was laid on early diagnosis and immediate enforcement of rest in bed for 2 to 4 months. As a routine treatment sodium cacodylate was injected intravenously every day for six to twelve weeks.

Splenectomy.—Removal of the spleen in general haemic conditions, for example, in leukaemia and Gaucher's disease, though it has been performed in the past, has not been really successful. D. Polowe, however, reported a bacteriologically-proved case of subacute bacterial endocarditis in which the patient was well more than

20 months after the onset of symptoms; this was the only case to recover in the 15 recorded cases thus treated. In 12 of the cases the presence of the disease was not proved before splenectomy was performed. Polowe stated that a false positive Wassermann reaction may be given in subacute bacterial endocarditis.

Treatment

Sulphanilamide.—A case of bacterial endocarditis is reported by L. J. Solway and H. G. Pritzker in which the blood culture was positive for *Streptococcus pyogenes*. Sulphanilamide was administered orally and subcutaneously and the blood concentration maintained at 12 mg per 100 c cm. Three courses of treatment were given with no toxic effects. The results obtained were consistent with what might be expected at the bacteria-free stage of subacute endocarditis. The patient was discharged from the hospital 6 months after admission, and re-admitted 6 weeks later, when death occurred. The findings at necropsy showed the presence of a healing around the scarred valves and in the myocardium and healing focal glomerulo-nephritis, but active ulceration of the valves was present with the presence of large colonies of bacteria. Recent infarcts were present in the spleen and kidneys. It was apparent that the vegetations had remained unaltered by the treatment.

Gonococcal

Steiner and Walton estimate that about 150 cases of gonococcal endocarditis have been published, but that in only 48 cases have gonococci been obtained by blood culture. They reported a proved case with vegetations on the pulmonary valve, double parotitis, and jaundice; the parotitis was ascribed to secondary bacterial invasion. Gonotoxic jaundice is unusual and was thought to be due to toxic changes in the liver cells. Lichtman suggested that overaction of the reticulo-endothelial system causes rapid and extensive haemolysis, and damages the liver cells. H. Keil described a form of gonococcal bacteraemia with a characteristic haemorrhagic vesiculo-papular and bullous eruption which may suggest the fatal prognosis of gonococcal endocarditis. Positive blood cultures do not necessarily prove the existence of specific endocarditis, and in its absence the prognosis is good.

Capps, J. A. (1938) *Proc. Instn. Med., Chicago*, **12**, 219.

Keil, H. (1938) *Quart. J. Med., N.S.*, **7**, 1.

Lichtman, S. S. (1937) *J. Mt Sinai Hosp.*, **4**, 72.

Polowe, D. (1939) *Arch. Surg., Chicago*, **38**, 139.

Solway, L. J., and Pritzker, H. G. (1939) *Canad. med. Ass. J.*, **40**, 543.

Steiner, W. R., and Walton, J. J. (1937) *The Anniversary Volume Scientific Contributions in Honor of Joseph Hersey Pratt on his Sixty-fifth Birthday By his Friends*, Lancaster, Pa., p. 720.

Acute Bacterial Endocarditis

Morbid Anatomy

A. C. Allan studied the structure of vegetations in 24 cases of acute and subacute bacterial endocarditis by means of differential connective tissue stains. A typical vegetation is usually considered to be composed of 3 zones, but the bulk of each of these was found to consist of a necrotic zone beneath a layer of bacteria. Isolated clumps, fragmented strands, and segmented pieces of typical adult elastic and collagenous tissue were found scattered through this necrotic zone in both acute and subacute cases. These fibres represent a destructive rather than a reparative process. It is concluded that the bulk of a vegetation in acute or subacute bacterial endocarditis is derived from components of inflamed and fibro-plastically deformed valves and not from blood flowing over the valves. This point may furnish supporting evidence that tissue immunity is a factor in the production of bacterial endocarditis.

Allan, A. C. (1939) *Arch. Path.*, **27**, 661.

HEART DISEASES: MITRAL VALVE DISEASES

See also Vol. VI, p. 309.

Mitral Stenosis

Morbid Anatomy

C. G. Aronslein and L. Newman reported a case of ball thrombus in the left auricle in a woman, aged 43, with advanced mitral stenosis. It was round with a

diameter of 3.5 cm. without any pedicle, its surface covered with small elevations the size of a pin's point and had evidently long been loose in the left auricle. In the 31 collected cases the sex was given in 21, 17 being in females mainly in the fifth decade. The commonest symptom was dyspnoea; another prominent feature was a cadaveric coldness of the extremities.

Aronson, C. G., and Newman, L. (1939) *Arch. Path.*, **27**, 907.

HEART DISEASES: AORTIC VALVE DISEASES

See also Vol. VI, p. 329

Aortic Stenosis

M. Texon finds that calcified aortic stenosis is becoming more commonly recognized, and that it should be differentiated from angina pectoris and coronary thrombosis, the symptoms of which are simulated by it. The systolic blood pressure in the absence of complications would be expected to be low, with a slight elevation of the diastolic. Characteristic smallness of the pulse was observed, and a long, loud, rough systolic murmur, often transmitted to the vessels of the neck, was heard. The second aortic sound was frequently absent or greatly diminished. Gradual hypertrophy of the heart occurred. He emphasized the fact that an X-ray was of value in diagnosis. The calcified valve could be seen to produce small dense shadows, showing a rapid up-and-down movement. They were not projected outside the cardiac shadow, and deep inspiration produced no alteration. Visualization was best made at the right oblique view in the median line, or a little to the right of it, in the lowest third of the cardiac area. The mitral valve was not found to be involved. Some authorities hold that calcified aortic stenosis is not rheumatic in origin, but is a degenerative disease with a resulting deposit of calcium. Once symptoms have appeared the prognosis is poor, and a life expectancy of about one year may be expected when congestive heart failure becomes apparent.

A. W. Contratto and S. A. Levine analysed 180 cases of stenosis of the aortic valves, based on physical signs and calcification of the valves shown by the fluoroscope or necropsy, and showed that there was a definite history of acute rheumatic infection or of chorea in 57 (32 per cent), the average age was 52 years, the extremes being 13 and 81 years, males 108, females 72, average blood pressure 145 systolic, diastolic 84 mm. Hg, angina pectoris occurred in 41 (23 per cent) of the cases, and true syncope in 21, the commonest causes of death were congestive heart failure, sub-acute bacterial endocarditis, and sudden death. Necropsies showed that calcification of the valves did not involve the orifices of the coronary arteries.

Contratto, A. W., and Levine, S. A. (1937) *Anniversary Volume: Scientific Contributions in Honor of Joseph Hersey Pratt on his Sixty-fifth Birthday. By his Friends*, Lancaster, Pa.

Texon, M. (1939) *New Engl. J. Med.*, **220**, 992.

HEART DISEASES: HEART FAILURE

See also Vol. VI, p. 368, Cumulative Supplement, Key No. 659, and p. 20 of this volume.

Complications

Peripheral Gangrene

A. M. Fishberg called attention to the occasional development of symmetrical peripheral gangrene in cardiac failure without occlusion of the arteries supplying the part, and suggested that with severe congestive cardiac failure and extreme diminution in the cardiac output selective vasoconstriction occurs whereby less blood is distributed to the limbs and more to the brain and other vital organs. C. Bruce Perry and T. B. Davis supported this view by a case in the terminal stages of congestive failure in which there was symmetrical peripheral gangrene of the lower limbs shortly before death due to a vasoconstriction which leads to a redistribution as suggested by Fishberg.

Fishberg, A. M. (1938) *J. clin. Invest.*, **17**, 510.

Perry, C. B., and Davis, T. B. (1939) *Brit. med. J.*, **1**, 15.

Treatment

Digitalis

H. J. Stewart *et al* (1938, a) investigated the action of digitalis on 17 patients suffering from compensated heart disease and having a normal sinus mechanism. 1.6 to 1.8 g. of digitalis were given within 24 hours and in all cases the T wave and R-T segment of the electrocardiogram showed characteristic changes of a digitalis effect. Observation on the cardiac output showed that in some cases in which the heart was made smaller it increased and in others it decreased. It was impossible to predict which effect would be produced. Digitalis has 4 clinical effects on the heart: (i) it increases the contraction, (ii) it decreases the size, (iii) it decreases the rate; and (iv) it has a typical effect on the electrocardiograph. In addition it increases the work done per beat by the heart whether it increases or decreases the output and whether the rhythm is regular or irregular. They concluded that the output is decreased by digitalis in normal persons and those without congestive heart failure because the heart is made smaller and not because the venous return is diminished.

Action of Digitalis

The action of digitalis in uncompensated heart disease was then investigated by H. J. Stewart *et al* (1938, b). In 20 cases of congestive heart failure the size of the heart was increased and the cardiac output decreased. The rhythm was regular in 11 of the patients and 9 had auricular fibrillation. The administration of digitalis resulted in a decrease in cardiac size due to an increase in tone, an increase in output, and a lowering of venous pressure if it was raised. The work per beat was also increased, and this, with the decrease in size of the heart, made the value of the work more nearly normal. They found that patients suffering from syphilitic or other cardiac lesions responded as well to digitalis therapy as rheumatics, and that it was just as efficacious in lesions of the aortic valve as of the mitral valve. The decrease in venous pressure was due to the increase in output and work per beat. Digitalis had the same action on the normal as on the damaged heart.

Digilamid

I. Rothlin has experimented with digilamid C, one of the glycosides extracted from *Digitalis lanata* (the common digitalis preparations are extracted from *Digitalis purpurea*). The main advantage of digilamid C over the other digitalis preparations is its good compatibility and its rapid effect if given by mouth. Digilamid C administered to cats produces a quicker effect and has a greater toxicity than the other components of the digilamid complex (digilamid A and digilamid B). The experiments prove that digilamid C is the most effective part of the digilamid complex. Digilamid C adheres much more to the heart muscle than other digitalis preparations with the exception of digitoxin which, however, is too toxic to be used in man. Digilamid C is more quickly absorbed and has a greater therapeutic breadth than the other components of the digilamid complex. The author recommends clinical tests.

L. Michaud also reported on the pharmacology of digilamid C, the effective part of the digilamid complex. Its advantages were its freedom from toxic effects, rapid action when taken by mouth, effect on the myocardium, and the wide margin between the therapeutic and the toxic doses. Digilamid C (dragées containing 0.25 mg. and ampoules for intravenous injection containing 0.2 mg. per c.cm.) was given to 20 patients with severe cardiac failure, and pulmonary and general stasis. The patients were kept completely at rest for some days with a restricted fluid intake, 3 patients experienced gastric disturbance while taking the dragées. The first effect of digilamid C was diuresis with rapid reduction of oedema and weight. Three cases on 6 to 8 dragées daily showed diuresis, in one from 600 c.cm. before treatment to 5,500 c.cm. on the fourth day of treatment, a remarkable fall of the pulse rate and of weight from 76, 87, and 71 kilos to 64, 79, and 63 kilos respectively in 10 days. The same effect followed the daily injection of 2 c.cm. of the solution (0.4 mg. of digilamid C), in one case the injection was followed in 2 hours by remarkable diuresis, which could not have been achieved with any other digitalis preparation. The rapid action of digilamid C resembled that of strophanthin but was not attended by the corresponding disadvantages. The pulse rate and blood pressure fell and became regular. Four patients were given about 100 dragées in one

day and 200 dragees in 2 days without any toxic symptom, the same was true as regards intravenous injections.

Michaud, L. (1938) *Schweiz. med. Wschr.*, **68**, 1338.

Rothlin, E. (1938) *Schweiz. med. Wschr.*, **68**, 1336.

Stewart, H. J., Dietrick, J. E., Crane, N. F., and Thompson, W. G. (1938, a) *Arch. intern. Med.*, **62**, 547.

— — — and Wheeler, C. H. (1938, b), *ibid.*, **62**, 569.

HEPATO-LENTICULAR DEGENERATION

See also Vol. VI, p. 443

Clinical Picture

I. J. Goldbach reports 3 cases of hepato-lenticular sclerosis showing the Kayser-Fleischer ring; 2 of them were brother and sister. Ophthalmological examination of the male case revealed absence of ptosis, nystagmus, and exophthalmos. Vision 20/15 O.U. A greenish-yellow pigment ring was seen to encircle the cornea just within the corneo-scleral margin. It was uniform and approximately 2.5 mm wide. The cornea was otherwise clear. Pupillary reactions and ocular movements were normal; ophthalmoscopic examination revealed normal nerve heads and fundi. The female case disclosed a Kayser-Fleischer ring similar to that in the case of her brother, but the ring was not so well developed. Abdominal examination of the male revealed absence of liver dullness in the mid-clavicular line. In the anterior axillary line, the dullness measured 7 cm from the 5th to the 7th interspace, and in the mid-axillary line it measured 6 cm from the 6th to the 7th interspace. In the female case, the lower edge of the liver could just be felt. Liver dullness was not increased. The third case reported was of the so-called atypical type. Examination of the eyes showed evidences of recent iritis in the left eye with posterior synechiae and old P.K. deposits. The vision, which had been corrected, was R.E. 20/30 and I.F. 20/200. There was a moderate degree of tuberculin sensitivity but no improvement was obtained under tuberculin therapy. Subsequently there was a sharp loss of vision in both eyes and periods of diplopia. There was no history of iridescent vision. The development of neurological symptoms was manifested by a dragging sensation in the right leg and unsteadiness of gait. The patient showed a positive Romberg sign, loss of vibratory sense and of passive movement of the legs, with increased knee- and ankle-jerks and bilateral extensor responses. Later, examination of the eyes showed an acute secondary glaucoma of the right eye with hazy cornea, iris bombé, posterior synechiae, and media so cloudy that the fundus could not be seen. Vision was reduced to R.E. 2/100, I.F. 15/100. This patient ultimately showed a definite dystrophy of both corneae with a greenish hue in the lower and deeper layers. The general physical examination was negative except for the ocular and neurological findings. As in the case of the others laboratory findings were negative.

Goldbach, I. J. (1938) *Amer. J. Ophthalm.*, **21**, 1118.

HERNIA

See also Vol. VI, p. 470, and Cumulative Supplement, Key Nos. 672-687

Inguinal Hernia

Direct Form

W. G. Gill drew attention to a type of direct hernia in which the posterior wall of the inguinal canal, internal to the deep epigastric artery, showed a small circular deficiency with firm, almost tendinous, margins, through which a tubular process of peritoneum, indistinguishable on clinical examination from an indirect hernia, escaped, often emerging through the external ring. It was uncertain if the hernia was congenital, due to some trauma, or caused by a localized extraperitoneal lipoma which weakened the fibrous sheet at one spot. A personal series of 80 herniae contained 3 cases of this type. In these the inguinal canal was normal in all respects, except for a localized opening in the transversalis fascia, with quite definite edges,

which would not admit more than the tip of the index finger. This form of hernia could only be recognized at operation. The bladder often forms part of the sac and must be stripped off from it. Particular attention must be paid to the suture of the opening in the transversalis fascia (See Fig. 15.)

Treatment

Prognosis of injection treatment—F. W. Slobe discussed the results attending the injection treatment of hernia and contrasted them with the results from surgery. He is inclined to consider that the degree of recurrence from operations on direct hernia over a period of 5 years may be as high as 25 per cent, while with indirect the figure is 5 per cent for the first year with an additional 1 per cent for each succeeding year. He thinks that too short a period has elapsed to enable us to completely gauge the success of the injection method, and points out that, since there is no set time when the treatment can be said to be completed, and further injections are usually necessary after an interval, there is a tendency to interpret a bulging as a sign of unfinished treatment. He is therefore inclined to discount partially claims made for a 95 per cent cure rate. In a group of 25 patients whom he studied after one series of injections, who wore a truss for 6 months and who received no further injections within 18 months, recurrence occurred in practically 50 per cent. Recurrences in general are smaller than the original hernia and may give no symptoms. To avoid them he is of opinion that repeated injection may have to be given for years, the truss being worn indefinitely.

Gill, W. G. (1939) *Brit med J.*, 1, 263

Slobe, F. W. (1939) *Amer J Surg*, 42, 704

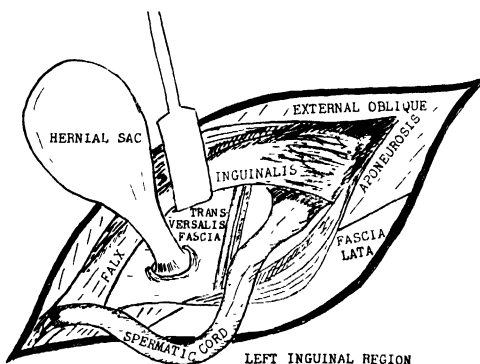


FIG. 15 Direct inguinal hernia: a diagrammatic drawing of the condition described by Gill. No attempt has been made to illustrate the bladder that forms part of the medial wall of the sac. The epigastric vessels are exaggerated in size and clarity in order to point out their relation to the sac. (From *The British Medical Journal*, 1939)

HERPES

See also Vol VI, p. 513

Herpes Simplex

Actiology

I. M. Burnet and S. W. Williams accept the view that herpes simplex is a specific infectious disease due to an exogenous virus, and support their contention with the fact proved by Dodd *et al.* that the common aphthous stomatitis found in young children is a herpetic infection. From observations and investigations the authors contend that antibody appears in early childhood, and the population may be regarded as becoming either potentially herpetic or non-herpetic for the rest of life. Herpes once contracted appears to remain for life though the virus is latent. Lesions may periodically appear, probably as the result of local trauma or fever. Antigenic stimulus is supplied by the virus, thus maintaining the antibody at a high level, which may not however prevent the occurrence of local herpes. The non-herpetic, although exposed to infection, possesses powers of resistance which enable him to resist exposure. Infants are considered to be highly susceptible to the virus of herpes simplex, and may become infected by virus liberated from the lesion of an adult or from a primary lesion in another child. The majority of herpetics were found amongst the class attending public hospitals. The fact is emphasized that this virus lives symbiotically in man, and that B virus and pseudorabies are members of the same stock which pursue a similar type of existence in monkey and pig respectively.

Morbid Anatomy

F. M. Burnet and D. Lush studied the content of human sera in antibodies against the herpes virus. They regard herpes simplex as being spread by droplet or salivary infection often between the ages of one and three and a vesicular stomatitis as the first clinical symptom. Once infection has occurred the virus may persist in the body for life. Its site is disputed but it may (i) reside in the central nervous system or probably, in labial herpes, in the Gasserian ganglion; (ii) persist in the epithelial cells of the buccal cavity. The virus cannot be demonstrated by inoculation methods in the Gasserian ganglia of individuals with high titre antibody in their serum. Cases of early poliomyelitis show no detectable herpes antibody.

Differential Diagnosis

E. V. Ullmann distinguishes between herpes febrilis and herpes genitalis. The latter, as its name implies, is confined to the genitals, is associated with the period of active sex life, and is accompanied by neuralgic pain and a mild lymphadenitis. Febrile herpes, on the other hand, is not accompanied by neuralgia or swelling, and, although the lesions may occasionally occur in a similar situation, certain characteristics peculiar to herpes genitalis are lacking. The most striking difference is that when febrilis is inoculated into the human skin a lesion occurs at the exact site of inoculation, but herpes genitalis appears at a short distance from the inoculated area. Herpetic laryngitis is a form also associated with pain and swelling and tends to be recurrent. Four cases of herpes are reported in which vaccination produced what appeared to be a cure, in that there was no recurrence over a period of years. The author wonders whether this result was obtained by actual immunization or merely by suggestion in the same way that laryngeal papillomas and warts sometimes disappear.

Treatment

Moccasin venom.—Fifteen patients with herpes simplex were treated by R. J. Kelly with moccasin venom. A dilution of 1 in 3,000 was administered intradermally in 0.2 c.c. doses. Local reaction was mild and at no time were constitutional symptoms noted. It was concluded that if the injections are given early in the course of the disease, i.e. from 8 to 24 hours after onset, the symptoms disappeared within 12 to 36 hours, leaving only small dry crusts, with no exudation. When the injection was given later in the disease little or no apparent change occurred. This therapy seemed to decrease the number of recurrences. Attempts to influence the virus directly by the use of moccasin venom in a 1 in 3,000 dilution in experiments on rabbits were unsuccessful.

Burnet, F. M., and Lush, D. (1939) *Lancet*, **1**, 629.

— and Williams, S. W. (1939) *Med. J. Aust.*, **1**, 637.

Kelly, R. J. (1938) *Arch. Derm. Syph.*, N.Y., **38**, 599.

Ullmann, E. V. (1939) *Northw. Med.*, Seattle, **38**, 15.

Herpes Zoster*Complications*

Encephalitis.—J. H. Biggart and J. A. Fisher describe the case of a man aged 63 who died of encephalitis about 6 weeks after the onset of typical herpes zoster. Histological examination showed a dorsal-root ganglionitis and a posterior myelitis in addition to the encephalitis. The authors suggest that the encephalitis was caused by the infective agent of the herpes zoster.

Treatment

Vitamin B₁.—H. Rattner and H. C. Roll have used vitamin B₁ in the treatment of 16 cases of herpes zoster. Crystalline thiamin chloride in doses of 2,000 international units was injected subcutaneously every second or third day. After the first injection a number of patients were already free from pain, but some of them required 6,000 units before improvement was noticeable. On the whole, however, the authors concluded that vitamin B₁ did not strikingly improve or cure this condition and only temporary improvement was obtained.

Procaine.—S. Rosenak treated 22 patients with herpes zoster by injection of 0.5 per cent procaine hydrochloride solution into the intervertebral and prevertebral ganglia. Each intervertebral ganglion and the prevertebral sympathetic cord were injected, 8 c.c. being used for each segment. The injection was given from 2 to 10 days after the appearance of the eruption. Except in 2 patients, the pain diminished

and the vesicles dried up in 24 to 48 hours. In 2 patients with trigeminal zoster, the Gasserian ganglion was infiltrated with 1 c cm. and 2 c cm. respectively of this dilute solution and in 2 days the symptoms disappeared

Biggart, J. H., and Fisher, J. A. (1938) *Lancet*, **2**, 944

Rattner, H., and Roll, H. C. (1939) *J. Amer. med. Ass.*, **112**, 2585

Rosenak, S. (1938) *Lancet*, **2**, 1056

HODGKIN'S DISEASE

See also Vol. VI, p. 523, and Cumulative Supplement, Key No. 691.

Clinical Picture and Prognosis

Functional State of Gastric Mucosa

Patients with Hodgkin's disease were examined by F. Harvey in order to determine the functional state of the gastric mucosa and the previous dietetic history. In 5 successive patients with glandular or splenic enlargement, there seemed to be evidence of damage of the stomach by strong tea, alcohol, tobacco, or excessive food. Their diet was very deficient in vitamins. In 4 out of the 5 cases there was complete achlorhydria, and in the fifth case, though free hydrochloric acid and total acid were present in normal amount, the patient's blood pointed to pernicious anaemia.

Effect of Sex on Prognosis

F. Epstein collected records of 204 cases of Hodgkin's disease in women and a series of 180 cases in men. Of the women more than three-quarters live more than 3 years after the first appearance of the disease, over 50 per cent survive more than 5 years, and nearly 20 per cent still live after 10 years. The percentage of women living more than 5 years is greater than that of men living 3 years. The age of onset is the same in the 2 sexes. The author considered that the findings suggest that women have some protection from Hodgkin's disease and that the catamenia and child-bearing have some influence on the prognosis.

Epstein, F. (1939) *Amer. J. Cancer*, **35**, 230

Harvey, I. (1938) *Brit. med. J.*, **2**, 833

Diagnosis and Differential Diagnosis

Gordon's Test

J. B. McNaught investigated the contention of Gordon that intracerebral inoculation of rabbits and guinea-pigs with suspensions of lymph nodes from patients with Hodgkin's disease produced a characteristic encephalitic syndrome. The original work furnished positive results in 19 out of 20 patients suffering from Hodgkin's disease and negative in 41 controls. It was therefore concluded that the test was specific for the condition. McNaught found that the test was positive in 10 out of 13 cases (77 per cent), and negative in 95 per cent of other lymphadenopathies. In both the patients with Hodgkin's disease and the control group, those cases giving a positive reaction were those in which there were numerous eosinophils in the glands. McNaught stated that the incidence of positive results of the test is equal to the incidence of eosinophils in Hodgkin's disease, and therefore is no better guide to the diagnosis of that condition.

McNaught, J. B. (1938) *J. Amer. med. Ass.*, **111**, 1280.

Treatment

X-irradiation

In what he called the third stage of Hodgkin's disease, namely, when the disease is generalized with visceral involvement, W. M. Levitt described the satisfactory results obtained by regional irradiation or 'X-ray baths' which may be thoracic, abdominal, or trunk (the two former combined). Trunk baths are not without danger and are only given to selected cases. When the liver and/or the spleen or upper abdominal glands are involved as well as the thoracic contents, the thoracic and upper abdominal bath is employed. High-voltage rays are used with appropriate filtration and protection above the upper, and below the lower, limit of the fields to be exposed. Careful blood-count control of the treatment is maintained. Very small doses are given at first, and these are gradually increased until the patient is

receiving daily doses of a high potency. Some hundreds of patients have been treated by thoracic or abdominal baths without an accident or death due to the treatment. One or 2 patients, however, died as the direct result of the trunk bath.

Levitt, W. M. (1938) *Brit. J. Radiol.*, N.S. **11**, 183.

HYDATID DISEASE

See also Vol. VI, p. 538

Aetiology

Geographical Distribution

O. J. Ofteigsson, an Icelandic, points out that the statement of the frequency of hydatid disease in Iceland, however true years ago, is no longer correct. In 1867 with a population of 69,000 there were 1,300 persons infested, whereas in 1920 with a population of 95,000 there were 36 cases only. This is due to very efficient prophylactic measures.

Ofteigsson, O. J. (1937) *Proc. Mayo Clin.*, **12**, 420.

Primary Cysts

Diagnosis of Rupture

É. Sergent *et al.*, while recognizing the value of Casoni's intradermic injection of hydatid fluid for the diagnosis, often difficult, of hydatid disease, drew attention to two limitations of practical importance. A case of multiple hydatid cysts in the lung had the test performed on 4 occasions, the first 3 tests done with hydatid fluid containing formal as an antiseptic were negative, whereas the fourth test with hydatid fluid not containing an antiseptic was positive. It would therefore appear that in the technique of the test the addition of an antiseptic to the hydatid fluid used for the test should be avoided. The second limitation was that the first time that the test is performed on a patient with hydatid fluid (without an antiseptic) is valuable, but that subsequent tests may give a fallacious positive result because the patient was sensitized by the fluid injected at the first test, and therefore should not be regarded as decisive.

Sergent, É., Fourrester, M., and Galliano, I. J. (1939) *Bull. Acad. Méd. Paris*, **121**, 180.

Hydatid Cysts in Central Nervous System

Eight cases of hydatids in the vertebral column were observed by O. Lugue and C. Brandian Caraffa since 1930, one at necropsy and the others at operation. The hydatids were outside or inside the dura mater. They never produced any alteration which could be established by X-ray examination. Clinical signs did not differ from those of compression of the spinal cord produced by other causes. Infiltrated vessels in the vertebral column were seen on microscopical examination in the case which came to necropsy. X-ray examination, however, showed no abnormal sign. Hydatids were not seen outside the vertebral column, at least X-ray examination did not demonstrate any abnormality.

Lugue, O., and Caraffa, C. B. (1939) *Arch. argent. Neurol.*, **20**, 12.

HYDROTHERAPY

See also Vol. VI, p. 573

Hot-Water Baths

In an account of the external uses of water in chronic rheumatic conditions, Drury Pennington divided the cases into sthenic and asthenic. His advice was more for practitioners in isolated districts remote from spas and properly equipped physiotherapeutic centres. A 'hot bath' method of inducing artificial fever was described: the temperature of the water was from 100° to 105° F., and the technique consisted in wrapping the patient, on emergence from the bath, in a large warmed towel, and placing him or her in bed between warmed blankets with hot-water bottles; the patient is then allowed to sweat profusely for 10 minutes, after which a tepid

sponge-down is given with a solution of sodium bicarbonate and water. The patient is then thoroughly dried. Improvement, if it occurs at all, should be evidenced after a course of 12 such baths, given not more often than twice a week. Before this treatment the asthenic patient is gradually acclimatized to the temperature of the water and the duration of immersion. The more sthenic patient with periarticular fibrosis receives, in addition, a jet of cold water directed upon the affected joint. This contrast method of hydrotherapy is contra-indicated in menorrhagia, and in cases in which the peripheral circulation is palpably deficient.

Pennington, D. (1938) *Brit J phys Med*, **1**, 375.

Balneotherapy

Sulphur and Sea-Water Baths

A. Grusin organized a special department for treatment by sulphur baths mixed with sea-water. He tried this treatment on 200 patients with diseases of the heart. There were 15 patients with endarteritis obliterans. Every patient had on the average 10 baths. The patients were treated both in summer and winter. These baths had a good effect on patients with chronic myocarditis, chronic myocardiopathy, and cardiosclerosis in which the blood pressure was not above 140 and the heart in a state of compensation. In many cases these baths gave a feeling of well-being to the patient and the rhythm of the heart became normal in cases of extra-systolic arrhythmia. The dyspnoea diminished, the pain in the heart region disappeared, and the functional state of the cardiovascular system improved. Especially good results from the sulphur baths mixed with sea-water were noticed in patients with pain in the heart region of rheumatic origin and also in patients suffering from rheumatic and gouty polyarthritis and polyarthralgia. The 15 patients with endarteritis obliterans also felt better after these baths and could walk longer distances.

Grusin, A. (1939) *Urach Dveto*, **21**, 95.

Mud Baths

When there is organic disease of the cardiovascular system, mud baths may be harmful and should therefore be employed with great caution. M. Iasinovskii *et al.*, of the Rheumatic Clinic, Odessa, treated 950 patients with diseases of the joints, most of whom also suffered from diseases of the cardiovascular system. 209 patients with polyarthritis and cardiovascular disease were treated by these baths. Almost all patients received applications of mud (104° F. for 15 to 20 minutes) alternating with sea baths and carbon dioxide baths over a period of one month. The best results were obtained in cases of rheumatic polyarthritis. The authors conclude that (i) the treatment of polyarthritis and cardiovascular disease gives better results when mud applications alternate with carbon dioxide gas baths than when mud applications are given alone, and (ii) the cardiovascular symptoms are improved by this combined treatment.

Iasinovskii, M., Solomianny, B., and Kvalbasser, P. (1939) *Urach Dveto*, **21**, 91.

HYPERCHLORHYDRIA

See also Vol. VII, p. 1, Cumulative Supplement, Key No. 708, and p. 167 of this volume.

Treatment

Magnesium Trisilicate

Administration of magnesium trisilicate by C. Graham Reid to 24 fasting subjects caused a moderate reduction in gastric acidity in 15 minutes, the maximal reduction being reached in 30 minutes. This was maintained for approximately one hour, after which a gradual rise occurred until the original acid value was reached in 3 hours. The quantity of magnesium trisilicate employed was 2 g. in 25 c.cm. of distilled water. This result compared favourably with an alkaline mixture containing sodium bicarbonate 2 parts, calcium carbonate 2 parts, and heavy magnesium oxide 1 part, which caused a rapid fall in gastric acidity reaching its maximum in 15 minutes, after which a rise set in, with return to the original value in one and a half hours. Magnesium trisilicate administered after 4-hourly meals in uncomplicated duodenal cases, together with interval feedings every 2 hours, failed to give a persistent

achlorhydria, but it produced a reduction in acidity which was maintained for approximately 2 hours from the time of administration, at the end of which a rise occurred. By this means, however, the acid level was kept below its original value, except for a rise at mid-day during the test period. The use of magnesium trisilicate last thing at night has been found helpful for those patients who are awakened by epigastric pain. At the saturation-point with methylene blue, it is 17 times as active as colloidal kaolin, and produces no undesirable side-effects. Its use is suggested in cases of acute food poisoning.

Reid, C. G. (1939) *Amer. J. digest. Dis.*, **6**, 267.

HYPERIDROSIS

See also Vol. VII, p. 25.

Treatment

Surgical

It is noted by J. C. White that young nervous people not infrequently suffer from excessive sweating of the palmar and plantar surfaces and of the fingers and toes so that work and social activities are adversely affected. Medical measures are unsatisfactory in these extreme cases, and denervation is considered the ideal treatment.

The operation must be performed with special care so that section of the ocular fibres which results in Horner's syndrome may be avoided and the portion of the lumbar chain above the second lumbar ganglion must be left intact in the male as this governs the power of ejaculation. Warm, dry extremities result. The procedure is usually carried out bilaterally, the operation being performed in 2 stages, an interval of 4 days to a week elapsing between the operations.

White, J. C. (1939) *New Engl. J. Med.*, **220**, 181.

HYPNOTISM

See also Vol. VII, p. 34.

Uses of Hypnotic Suggestion

F. Dubnikov treated a series of nervous patients (216 females and 56 males) as well as 39 dipsomaniacs and smokers by hypnosis. The majority were between 30 and 40 years of age. There was an improvement in 71 per cent after treatment by hypnosis. Of 8 children with enuresis only 2 showed any improvement. Of 7 cases of eczema of nervous origin treated, 3 were cured and one showed improvement. Of 35 cases of 'acute reactive state' owing to the sudden death of a relative, or worries, 10 recovered completely, 7 showed great improvement, and 11 improved slightly. Of 80 patients suffering from hysteria, 18 were completely freed from their symptoms and 28 showed a great improvement. Of 49 psychasthenics 17 were much improved. Of 39 dipsomaniacs and smokers 2 dipsomaniacs ceased to drink, 3 lost much of their desire to drink, 7 ceased to smoke entirely, and 9 decreased their smoking to a few cigarettes each day. Of 36 cases of insomnia, 16 recovered completely and 8 showed marked improvement.

Dubnikov, E. (1939) *Sovetsk. vrach. J.*, **43**, 109.

HYPOGLYCAEMIA AND HYPERINSULINISM

See also Vol. VII, p. 42, Cumulative Supplement, Key No. 712, and p. 72 of this volume.

Artificial Hypoglycaemia

Morbid Anatomy

A. B. Baker discussed certain cerebral changes occurring as the result of artificial hypoglycaemia. Two case reports are given together with the findings at necropsy, and in each there were 3 outstanding cerebral changes: (i) cerebral petechiae, these ranged from small extravasations to large haemorrhages; (ii) large areas of encephalomalacia, demyelination and cyst formation; (iii) diffuse generalized glial prolifera-

tion and extensive gliosis around the areas of softening. It was apparent that a single one of these conditions or a combination of them would be sufficient to produce severe lasting injury, permanent functional damage or, perhaps, death. The author thought that such treatment should be undertaken with caution.

Baker, A. B. (1938) *Arch. Path.*, **26**, 765.

Spontaneous 'Hypoglycaemic Encephalopathy'

Clinical Picture

F. T. Rembom gave an account of spontaneous 'hypoglycaemic encephalopathy' in a brother and sister who both disliked sweet foods. The appearance of the sister, aged 52, somewhat resembled that of Cushing's syndrome, and her attacks had been regarded as due to some ovarian dysfunction, but they had continued after both hysterectomy and the menopause. The carotid sinus mechanism was normal in both cases.

Rembom, I. T. (1938) *Brit. med. J.*, **1**, 1087.

Functional Hyperinsulinism

Treatment

Partial pancreatectomy. J. M. Clarke reviewed the literature of functional hyperinsulinism, many of the cases being associated with pancreatic tumours. Glucose tolerance tests show that in this condition an increased carbohydrate intake results in an increased production of insulin, and the blood-sugar becomes low. Administration of carbohydrate and insulin together does not appear to prevent this excessive production of insulin. A rise in blood-sugar has been produced by starvation and by giving adrenaline or pituitary extract when reserves are present in the liver. A low blood-sugar does not usually produce symptoms until it has reached 65 mg. per 100 c.c.m., and at 40 mg. coma supervenes. Functional hyperinsulinism may be due to pancreatic tumour, hypertrophy of the islets (when the condition may be treated by partial pancreatectomy), or hypofunction of the anterior lobe of the pituitary. If partial pancreatectomy is performed, it is necessary to remove a large amount of the gland as removal of a small amount does not effect a cure. The author reported a case occurring in a man of 30 years which was successfully treated with partial pancreatectomy.

Clarke, J. M. (1938) *Aust. N. Z. J. Surg.*, **8**, 66.

ICHTHYOSIS

See also Vol. VII, p. 52.

Rud's Syndrome

Clinical Picture

R. M. Stewart presents a case related to Rud's syndrome characterized by ichthyosis, mental deficiency, and epilepsy with the additional features of arachnodactyly, retinitis pigmentosa, and muscular atrophy. Van Bogaert reported two other similar cases in 1935 and concluded that the syndrome of Rud is closely allied to xerodermic idioey and palmo-plantar keratosis with a precocious arteriosclerosis of the nervous system, and must be included as a congenital neuro-ectodermal dysplasia similar to tuberous sclerosis or neurofibromatosis. Histological examination of the brain in Stewart's case revealed that the changes resembled those found in idioey.

Stewart, R. M. (1939) *J. ment. Sci.*, **85**, 256.

IMMUNITY AND IMMUNIZATION

See also Vol. VII, p. 58, and Cumulative Supplement, Key Nos. 720-733.

Vaccines

Shock Reactions

G. T. Brown described constitutional reactions due to injections of bacterial vaccines, these were definite shock reactions comparable to that produced inten-

tionally by intravenous injection of antityphoid vaccine in protein-shock treatment. Half an hour or later after injection the onset of symptoms occurred with a chill and sometimes, especially in children, with nausea and vomiting, fever, malaise, aches and pains, thus resembling the onset of influenza. It was regarded as due to accidental injection into a blood vessel, and local reaction was either negligible or absent, because some or all of the vaccine had been abruptly carried away from the site of injection. The following precautions were recommended to prevent such constitutional reactions: because of its poor vascularity, the outer part of the upper arm, about half-way between the shoulder and elbow, should be chosen for the injection; after the needle has been inserted, but before any vaccine is injected, the piston of the syringe should be sharply retracted and, if blood appears, the needle must be withdrawn and inserted elsewhere, and the process repeated, the vaccine must be injected slowly and, if large in amount, the piston of the syringe retracted several times during the injection to make certain that the tip of the needle has not slipped into a small vessel. When the injection is completed, a pledget of cotton-wool, moistened with alcohol, should be pressed over the injection site while the needle is withdrawn, and for some time after, to prevent vaccine tracking back through the needle wound into any superficial vessel that might have been punctured by the needle. The treatment of the shock reaction consists of the oral administration of ephedrine and amylal, or ephedrine and phenobarbitone, and rest in bed during the short febrile period.

Brown, G. T. (1938) *Ann. intern. Med.*, **12**, 493.

Practical Applications

Enteric Fevers

Vi-antigen.—S. S. Bhatnagar discussed the alteration in the diagnostic significance of a Widal reaction since it has become known that the typhoid-paratyphoid group of organisms are possessed of more than one antigenic component: notably the flagellar H-antigen and the somatic O-antigen. The great majority of strains of *Bact. typhosum* possess a third antigen—the Vi-antigen described as such by Felix and his co-workers. Serological analysis over the past 3 years from patients suspected to be suffering from typhoid fever suggests that Vi-agglutination may be a more reliable method of diagnosis than the other types. When an organism with the morphology and the biochemical reactions of *Bact. typhosum* is found to agglutinate with a typhoid O serum much below the established titre of the serum, the presence of Vi-antigen in the culture is to be suspected. This is confirmed if it gives a positive reaction in agglutination with a pure Vi-serum—e.g. a serum from which O- and H-antibodies have been removed by adsorption. In a series of 134 cases, the serum from each case was collected every fourth day and titrated for the presence of the 3 types of antibody. Vi-antibody was present in the serum from every case of typhoid, whether inoculated or not. Inoculated individuals generally gave a higher reading. In the inoculated the rise of the Vi-agglutinin curve was steeper, more Vi-antibody was produced, and the highest point was reached much earlier (on the tenth day). In the uninoculated the rise was much more gradual, and the highest titre (only 1 in 50 compared with 1 in 100 of the inoculated person) was not reached until the eighteenth day. Among an inoculated community a definite conclusion can be reached by the end of the first week. In an uninoculated community, frequent tests will detect the presence of this antibody at a titre of 1 in 10 to 1 in 25 during the second week. In this series there has been no failure to correlate a positive Vi-agglutination reaction with either the isolation of the infecting organism or with a positive clinical picture of typhoid fever, in which bacteriological proof of the presence of typhoid infection could not be obtained. For the quantitative estimation of the Vi-antibody, a type of tube with a round bottom, such as is employed in Felix's technique for the differentiation of O and H, is used. The tubes are about 5 cm. long and have a uniform internal diameter of about 1.25 cm. During convalescence from typhoid fever only traces of Vi-antibody could be found in the serum. In a certain number of cases, however, the Vi-titre continued to be high in spite of the termination of the acute infection. Investigations showed that this variation connoted a tendency toward the typhoid-carrier condition. The detection of Vi-antibody in a serum is taken to be an indication for a thorough search for typhoid bacilli in the stools and urine.

Bhatnagar, S. S. (1938) *Brit. med. J.*, **2**, 1195.

IMPETIGO

See also Vol. VII, p 81, and Cumulative Supplement, Key Nos 734 and 735.

Treatment*Uleron*

G. Zederbauer demonstrated the use of uleron in the treatment of severe impetigo in children. The 3 patients treated by him were all chronic recurrent cases, reacting only with difficulty to the standard methods of treatment, and not healing after any previous course of treatment. The author treated these 3 specially severe cases of impetigo with uleron, and, in 7, 8, and 9 days respectively, the condition was completely cured, and did not recur after a period of observation. The action of uleron is chiefly that it enables the leucocytes to exert their phagocytic action on the micro-organisms; this can only be achieved if a constant level of the drug is maintained in the blood. 2 to 4 tablets, 3 or 4 times daily, is the standard dose recommended by the author, and special emphasis was laid on the administration of a late evening dose to prevent a nocturnal fall in the level of the uleron in the blood. Local treatment was unnecessary in two of the cases, but a neutral ointment can be applied.

Coffee Beans

H. Mommsen reported two cases, the one a torpid resistant ulcer of the leg, the other a seborrhoeic dermatitis complicated by impetigo, which were successfully treated by coffee beans. The pulverized coffee beans were strewn on to the surface of the lesions, and the ulcer healed in six weeks, while the dermatitis improved within a few weeks. In the latter case a restricted diet was maintained for over 11 days.

Mommsen, H. (1939) *Med. Klinik*, **35**, 784.

Zederbauer, G. (1939) *Wien klin. Wschr.*, **52**, 459.

INFANT FEEDING: THE FEEDING OF NORMAL INFANTS
AND CHILDREN

See also Vol. VII, p 136, and Cumulative Supplement, Key Nos 749-753.

Principles*Properties of Milk*

W. Catel had previously proved that heating milk reduced its biological value and that its intake diminished the natural immunity of infants, and caused dyspepsia and tetany. It appeared that some important constituents of the milk might either be destroyed, or their absorption hindered. When fresh human milk was allowed to stand the amount of vitamin C was rapidly reduced from 1.10 to 0.14 mg. per cent after one hour in the sun, to 0.32 mg. per cent after 10 hours in diffuse daylight, and to 0.99 mg. per cent after 10 hours in a refrigerator. When fresh human milk was heated for 3, 5, and 10 minutes, the vitamin C content was unchanged after 3 minutes, but increased to 1.38 and 2.33 mg. per cent after 5 and 10 minutes respectively. It was suggested that part of the vitamin normally fixed to protein was freed. Inhibins present in fresh cow's and human milk suppressed the growth of organisms. Diphtheria bacilli and streptococci did not grow on 50 per cent fresh-human-milk-agar, but grew profusely on a 50 per cent cooked-human-milk-agar. Staphylococci and pneumococci grew only to a very small extent on the fresh-milk culture, but multiplied abundantly on cooked-milk-agar. The growth of *Bact. proteumans* and *Bact. coli* was not hindered by fresh milk. Fat was digested in infants mainly with the aid of the lipase of the milk, as the action of gastric lipase was somewhat feeble. The lipase in human milk was destroyed after one minute's heating to 74° C. Phosphatase and citric acid were also very rapidly destroyed by cooking. The destruction of the lipase caused food to remain in the stomach a long time with consequent dyspepsia, and destruction of inhibins reduced the natural immunizing powers of the organism.

Vitamin C

C. E. Snelling and S. H. Jackson measured the vitamin C in the plasma of pregnant women. The ascorbic acid content of the blood seems to fall towards the end of pregnancy, and it is assumed that factors associated with labour are responsible for this fall. The greater part of the maternal vitamin C reserve is used up by the foetus, which acts as a parasite, foetal blood has far higher levels of vitamin C than maternal blood. For a breast-fed baby 4 mg. per cent of ascorbic acid in the milk is the minimal requirement, but deficiencies do not appear as long as the level does not sink below 2 mg. Babies receiving artificial food should be given an extra supply of vitamin C. If there is a vitamin C deficiency in the mother's diet, this must be corrected in the case of breast-fed babies.

Catell, W. (1935) *Dtsch. med. Wschr.*, **61**, 985.

(1939) *Klin. Wschr.*, **18**, 342.

Snelling, C. E., and Jackson, S. H. (1939) *J. Pediat.*, **14**, 447.

Artificial Feeding*Honey in Diet*

F. W. Schlutz and E. M. Knott discuss the importance of honey as a food in infancy and for growing children, and find that its value lies in its combination of 40 per cent laevulose, 34 per cent glucose, 1.5 per cent dextrin, and 1.9 per cent sucrose, which are most acceptable to the body, in addition it contains iron, copper, and manganese. The unique conjunction of dextrose and laevulose results in rapid absorption, without flooding of the blood stream with exogenous sugars, and also in the maintenance of a steady and slow decrease until the fasting level is again reached. Ten healthy male infants were studied, during their first 6 months, for a total of 151 weeks. It was found that honey was easily digested, well tolerated, encouraged a gain in weight, and did not produce diarrhoea. It was superior to karo corn syrup as a source of carbohydrate.

Banana in Diet

J. D. Craig reviewed the results of feeding 444 bottle-fed infants with ripe banana as a complement to the diet. The banana was measured in inches, one inch yielding approximately 18 to 20 calories, it was mashed and given separately from the milk diet. Each infant started with one inch, and the amount was increased according to the infant's desire for it. Orange juice was also given, but no other solid food. The banana diet was begun at the age of 6 weeks, and found to be easily digestible. It was useful as an introduction to solid food. Cod-liver oil was used in all cases. All the infants in this series were underweight or had complicating illnesses, but the incidence of gastro-intestinal irritation and diarrhoea was low, possibly because less carbohydrate was needed in the diet when banana was used to supplement it. One group of infants, fed on banana immediately after the cessation of diarrhoea, assimilated it well and diarrhoea did not recur. The infants who were underweight gained, but the author received the impression that the amount of weight gained was less than might have been expected from the combined calorie value of the milk and banana. The fruit was neither constipating nor laxative.

Apple in Diet

In the past cows' milk has been modified to approximate to breast milk (i) by raising the hydrogen-ion concentration and reducing the buffering capacity, and (ii) by producing 'soft curd' milk by diluting or heating the milk. Apple contains malic acid which lowers the pH, and pectin which reduces the curd tension of milk. F. J. Reithel and I. A. Manville found that the addition of apple alone lowered the initial pH, and that addition of lactic acid also reduced the pH from 7.0 to 3.9. The effect of hydrochloric acid in lowering the pH was increased by the presence of apple. Apple also made the curd finer, softer, more fragile, and more flocculent. The colloidal nature of pectin keeps the curd in suspension, in which state it is more susceptible to the action of digestive enzymes. From clinical observation it is advisable, when cows' milk is digested with difficulty, to use milk to which 4 or 5 per cent of dried apple has been added.

I. A. Manville described his method of adding apple to milk formulas for the feeding of infants and invalids. If the babies' formula is being built up from cows' milk, he used a good brand of evaporated milk diluted to twice its volume with water containing 10 per cent of apple powder. The formula thus contained 5 per cent of apple powder. The water is prepared by putting 2 moderately heaped tea-

spoonfuls of apple powder in an 8-ounce water container. For older children and adults all food was withheld for 3 to 4 days, during which an apple powder was given at 3 to 4 hourly intervals. After this, the diet was increased by giving custards containing 5 per cent of apple powder, and jellies containing 15 to 20 per cent. After 2 or 3 days buttermilk and cheese were added at times to the diet. The protein foods must be restored last and with caution. This treatment was found particularly efficacious in those suffering from 'intestinal influenza'

Craig, J. D. (1938) *J. Pediat*, **13**, 239

Manville, I. A. (1939), *Amer. J. Dis. Child.*, **57**, 167.

Reithel, F. J., and Manville, I. A. (1938) *Amer. J. Dis. Child.*, **56**, 235

Schlutz, F. W., and Knott, I. M. (1938) *J. Pediat*, **13**, 465

INFLUENZA

See also Vol. VII, p. 173, and Cumulative Supplement, Key No. 754

Bacteriology

Transmission to Animals

M. Tsurumi *et al* succeeded in transmitting the virus of influenza to the Korean squirrel, *Lutamus asiaticus orientalis*, a dilution of 1 in 1,000,000 was sufficient to transmit the disease. Mice were subsequently infected with the material derived from the lungs from the infected Korean squirrel and pneumonia developed in all of them.

A New Filtrable Agent

A new filtrable agent, associated with an unusual form of tracheo-bronchitis, was described by J. Stokes, Jnr., *et al*. The clinical features of this respiratory infection, often regarded as influenza, of which there was not any bacteriological evidence, were described at length by H. A. Reimann. The constitutional symptoms were severe. Laboratory experiments on ferrets and guinea-pigs, which were injected intranasally with cultures obtained from washings of the nose and throat of patients, produced cerebral symptoms, the lungs being normal. Injections intracerebrally and intranasally into Swiss mice caused cerebral and broncho-pneumonic changes. The virus was not that of influenza, lymphocytic chorio-meningitis, or of the meningo-pneumonitis described recently by T. Francis, Jnr., and T. P. Magill. Whether the virus was of animal or human origin could not yet be decided, but these observations suggested that a new filtrable agent had been found which caused disease in mice, guinea-pigs, and possibly ferrets, and also might have been in part responsible for the disease of the patients described.

Francis, T., Jnr., and Magill, T. P. (1938) *J. exp. Med.*, **68**, 147.

Reimann, H. A. (1938) *J. Amer. med. Ass.*, **111**, 2377.

Stokes, J., Jnr., Kenney, A. S., and Shaw, D. R. (1939) *Trans. Coll. Phys. Philad.*, 4th ser., **6**, 329.

Tsurumi, M., Ogasawara, K., and Takagi, H. (1939) *Nagoya J. med. Sci.*, **13**, 61.

INJURIES

Injuries in Parachute Landings

T. Dolbinin studied the type of injuries received in parachute landings. Over a period of 4 years, out of 12,000 leaps, 128 resulted in injuries, i.e. 1.4 per cent. Most of the injuries were to the lower extremities or feet, though occasionally there were injuries to the pelvis, head, knees, and other parts. The majority were partial or complete fractures, sprains, or bruises, 77 per cent of the injuries were sustained by persons making their first or second jump, and were due to wrong technique in landing. For the prevention of such injuries as have occurred in parachute landings it is necessary to have suitable uniform and boots, and for the jumper to make a preliminary study of correct jumping and landing.

Dolbinin, T. (1938) *Vo.-sanit. Dvzlo*, **2**, 49.

Treatment

Antiseptics

Alcohol—It has been thought that whatever antiseptic action ethyl alcohol had on the skin was due mainly to detergent properties and not to any bactericidal power. P. B. Price has shown that ethyl alcohol, within certain narrow limits of concentration, is strongly bactericidal both *in vitro* and on the skin. He found that when the hands had been washed in sterile water, examination of that water showed the kind of organisms on which the alcohol had to act. The hands were then washed in alcohol and then once more in sterile water to determine how many organisms the alcohol had left on the skin. He found that alcohol could remove the organisms from the skin, and that the best solution to apply was a strength of 70 per cent by weight. Friction by scrubbing increased the speed of the "degermination." He also found that alcohol is not merely a fat solvent, for which purpose it is used to clear the skin before operation, but is also bactericidal. In strongly bactericidal concentration alcohol is not a fat solvent. Seventy per cent alcohol (by weight) rapidly destroys bacteria *in vitro*. It acts rapidly at first and then more slowly on remaining organisms. Both higher and lower concentrations of alcohol are less effective. On the basis of these experiments Price recommended that before operation the hands and arms should be scrubbed with soap and warm water for 7 minutes and then dried on a sterile absorbent towel. They should then be bathed in 95 per cent alcohol to remove any remaining water and scrubbed for 3 minutes with sterile gauze in 70 per cent alcohol (by weight). The hands are then dried again with a second sterile towel. The area of operation should also be cleansed with 70 per cent alcohol (by weight). It is important to remember that evaporation weakens and lessens the bactericidal power of this alcohol.

Lecarde, of Damascus, advocated the substitution of 95 per cent alcohol for tincture of iodine in the pre-operative preparation of the field of the incision. This he had practised with uniform success for 9 years in 5,100 major and 7,800 minor operations. It did not damage the cutaneous epithelium and delay cicatrization of the operative wound, as iodine might do, and should also be employed in the subsequent dressing of the skin incision. Since laboratory experiments had shown that alcohol was the best chemical preparation for the surgeon's hands, the author considered that patients should share this advantage.

Mercurochrome—Owing to the toxic results, such as diarrhoea, vomiting, and chills, following the intravenous use of mercurochrome in the treatment of infections and the occasional deaths reported, the practice has been largely abandoned. J. L. Emmett found in 22 cases that intravenous mercurochrome in smaller doses than were previously used (not more than 10 c cm. of a 1 per cent solution) was an excellent antipyretic in cases of protracted acute pyelonephritis. Ten of the cases occurred after operation and of the remaining 12 renal stones were present in some of them. The mercurochrome injection did not eradicate the infection, but terminated the fever and the acute phase of the disease. It was necessary to employ other chemotherapeutic agents to sterilize the urine. When septic fever threatens the life of a patient whose general condition is very poor, the antipyretic action of mercurochrome may save his life. It was found to be of special value when prolonged prostatic obstruction had caused severe renal disease. Emmett reported a case of pyelonephritis following resection of the prostate in which the temperature was reduced to normal with the injection of 5 c cm. of a 1 per cent solution of mercurochrome, and the patient subsequently recovered completely.

Metaphen.—E. Mayer and L. Arnold performed tests on various germicides which were used for sterilizing the oral mucous membrane and found that the anhydride of 4-nitro-5-hydroxymercuri-*ortho*-cresol (metaphen) 1 in 200 was the most satisfactory solution. Tincture of iodine (3.5 per cent solution) was irritating but efficient, while mercurochrome 5 per cent in 50 per cent alcohol was effective, having a selective action on *Staphylococcus albus*. Only very slight irritation resulted from the use of metaphen. Colonies were reduced 95 to 100 per cent in 5 minutes from the application. It remained effective for 2 hours and was easily removable by water, no subsequent effects being noted. It was found that streptococci were more resistant to all germicides than staphylococci, and returned earlier. The under side of the upper lip was the area of application, cotton rolls being used on both sides of the superior maxilla.

Mercury Compounds for Sterilization of Instruments—J. H. Brewer investigated the antibacterial effects of the organic compounds of mercury with special reference to

their use as germicides in the sterilization of surgical instruments. He found that none of the compounds sterilized instruments in the presence of spore-forming organisms. An examination of instruments actually revealed that 12 per cent in a series of 120 surgical operations were contaminated with spore-forming anaerobes and 8 per cent of the skin knives were contaminated with *Cl. welchii*. Some of the organisms, however, such as *B. anthracis*, were rendered non-infectious to mice by the compounds. The action of the compounds on some vegetative bacteria was found to be slower than is commonly supposed. One of the mercurials used did not kill *Staphylococcus aureus* in 30 minutes and none was capable of killing *Cl. tetani*.

Rideal-Walker test—A. C. Thaysen investigated the efficacy of the Rideal-Walker test for the evaluation of antiseptics. Discrepancies in the results of the test were found and attributed to the fact that there is present in every bacterial population a small number which survive the action of a disinfectant very much longer than the great majority. If the number of these survivors is reduced either by a longer exposure to the antiseptic, as in the Chick-Martin test in which the exposure is 30 minutes instead of the 10 minutes of the Rideal-Walker test, the results of the test became more uniform. The Rideal-Walker test, in allotting a certain coefficient value to an antiseptic, does not indicate that all the cells of a culture of *Bact. typhosum* added to the antiseptic have been destroyed after exposure for the appropriate time.

Zephiran—A mixture of alkyl-dimethyl benzyl-ammonium chloride (zephiran) was used with considerable success by L. T. Wright and R. S. Wilkinson in various cases in the casualty department of Harlem Hospital. Types of cases treated included wounds and deep lacerations, burns, amputations, and bone operations, the removal of foreign bodies in the extremities, and avulsions. The skin was prepared for laparotomy by washing with water, alcohol and ether, and finally with an aqueous solution of zephiran 1 in 1,000. Immediate pre-operative treatment consisted of the application of alcohol and the aqueous solution of zephiran 1 in 1,000 alternately, 2 or 3 times. The area was then painted with the tinted tincture of zephiran, 1 in 1,000. Similar preparations were made in all operative procedures. Deep wounds were irrigated with 1 in 1,000 or 1 in 5,000 solutions. Massive wet dressings were used in some areas. Zephiran was found to be non-irritant to the tissues, if used in the correct dilutions, and caused no damage to healing surfaces. It has proven germicidal properties, and is non-toxic.

Prophylaxis of Gas Gangrene

C. L. Callander *et al* believe that the prophylactic dosage of antiserum in cases which might develop gas gangrene is too small, and have seen cases terminate in gas gangrene in spite of such administration. When an examination of the wound reveals suspicious organisms, a second injection of antiserum should be given. One useful antiserum contains 10,000 units Welch antitoxin, 10,000 units oedematis maligni antitoxin, 200 units novyi antitoxin, 200 units Sordelli antitoxin, 25 units histolyticus antitoxin. The authors think that X-ray treatment has a measure of efficiency, but, as it is combined with the more established modes of treatment, it is difficult to be sure of any specific action.

Painless Closure of Wounds

M. Goss described a painless method of closure of wounds which he has used in about 30 cases, over a period of 2 years. Briefly, the technique consists of washing the wound and surrounding parts with soap and water, removing gross contamination and blood clots, and, where debris is present in the wound, inserting a rubber dam drain, which is brought out at one end and left in position for 24 hours. Next, the skin is painted with tincture of benzoin, and two pieces of adhesive tape are placed one on each side of the wound, parallel with it, and a quarter of an inch from the wound edges. The two adhesive strips are then sutured together with a continuous silk suture. When removal is necessary, the adhesive strips are loosened and removed, complete with sutures, at one movement.

Celluloid in Repair of Cranial Injuries

Because of absorption of the graft, the repair of cranial defects due to injury by various bone-grafting procedures is often unsatisfactory. A method for the repair of cranial defects following previous bone-grafting operations is described by K. W. Ney. A plate of celluloid, 0.06 or 0.075 inch in thickness, is pierced with holes $\frac{1}{8}$ of an inch in diameter and 1 cm. apart, and cut to the required size. It is then inserted into the defect. The outer table of the skull is chiselled so that the celluloid can be inserted as an inlay, the entire operation being carried out under the strictest aseptic

conditions with drainage; the drainage material is removed after 48 hours. The holes in the plate serve a twofold purpose; they permit the escape of any serum which may collect, and, in addition, the tissues grow through the apertures and anchor the plate firmly in position. The celluloid is sterilized by immersion for 4 hours in a 50 per cent solution of ethyl alcohol, and, after being dipped in warm water, may be bent to the required shape. It is non-absorbable. The author has performed 300 such operations, and in only 5 did infection necessitate removal of the plate, which in 4 cases was successfully re-inserted.

Human Oil in Adherent Scars

In adherent scars, more particularly those adherent to bone or cartilage, C. P. G. Wakeley obtained good results from the injection of human oil, which is liquid at body temperature but solid at lower levels. A portion of omentum, removed from a patient during laparotomy, is placed in a sterile vessel, washed with distilled water to free it as completely as possible from serum and blood, and then placed in a specimen jar half filled with distilled water and plugged with cotton-wool. The jar is then heated to 120° C. in the autoclave for half an hour. After this, most of the fat floats free on the surface of the water as a clear yellow oil. While still warm it is pipetted off with a sterile capillary pipette and distributed into sterile 1 c.cm. ampoules. A little is also inoculated into broth culture-medium to check its sterility. The ampoules are again sterilized within test-tubes after sealing, the exteriors thus remaining sterile. From the ampoule, the oil is withdrawn for injection into a warmed 5 c.cm. Record syringe. A site is selected just at the outer border of the scar tissue, and the syringe insinuated between the bone and the contracted and adherent skin. The oil is forced between these 2 structures, not more than 1 c.cm. being injected at any one place. The scar tissue is actually raised off the adherent bone or cartilage. Several areas can be injected at one sitting. About 24 hours after the injection, the site becomes red and hot, this condition persisting for about 12 to 24 hours, and then gradually disappearing. An interval of a fortnight should elapse between the sittings. By degrees the adherent scar is thus made to float upon the underlying structure. In badly adherent scars due to X-ray burns, as many as 20 to 25 injections may be required. Not more than 1.5 c.cm. should be injected in any one area. The advantage of the treatment is that the subject can attend as an out-patient, and it does not cause any incapacity. It often obviates extensive plastic operations.

Effect of Sulphamylamide on Healing of Wounds

E. M. Bricker and E. A. Graham published their findings on the effect of sulphamylamide on the healing of wounds in dogs and concluded that in uninfected wounds the period of healing, as judged by tensile strength, is lengthened.

Brewer, J. H. (1939) *J. Amer. med. Ass.*, **112**, 2009.

Bricker, E. M., and Graham, E. A. (1939) *J. Amer. med. Ass.*, **112**, 2593.

Callander, C. L., Haim, A., and Maximov, A. (1938) *Amer. J. Surg.*, **42**, 811.

Emmett, J. I. (1938) *J. Urol.*, **40**, 312.

Goss, M. (1939) *Amer. J. Surg.*, **44**, 400.

Lecard (1939) *Bull. Acad. Méd. Paris*, **121**, 760.

Mayer, E., and Arnold, L. (1938) *Amer. J. digest. Dis.*, **5**, 418.

Ney, K. W. (1939) *Amer. J. Surg.*, **44**, 394.

Price, P. B. (1939) *Arch. Surg., Chicago*, **38**, 528.

Thaysen, A. C. (1938) *J. Hyg., Camb.*, **38**, 558.

Wakeley, C. P. G. (1938) *Brit. med. J.*, **2**, 618.

Wright, L. T., and Wilkinson, R. S. (1939) *Amer. J. Surg.*, **44**, 626.

INSOMNIA

See also Vol. VII, p. 191, and p. 19 of this volume.

Aetiology

J. G. Schnedorf and A. C. Ivy repeated the experiments of Pieron concerning the hypnotoxin theory of sleep, and obtained results which to some extent furnished supporting evidence.

Eight c.cm. of cerebrospinal fluid were withdrawn from normal dogs in 3 minutes,

and replaced by 8 c.cm. of fluid from 'fatigued' dogs who had been kept awake and standing from 7 to 16 days. Cerebrospinal fluid from fatigued dogs depresses the central nervous system more than normal fluid, but does not produce normal sleep. In 9 out of 20 dogs, a depression of the cerebral nervous system, or 'sleep', was graded at 3 or 4 plus. Only 4 of 24 control dogs which received in the same manner either fluid from a normal dog, or their own fluid or normal saline solution, showed a 3 plus depression. The normal picture of sleep is not produced because the body temperature of both groups is elevated approximately 2.6° F. The rise produced in intracranial pressure cannot be a feature of primary importance in causing the onset of sleep, because, when 8 c.cm. of cerebrospinal fluid are withdrawn from a fatigued dog, such a dog will fall asleep in 5 minutes. In the case of a non-fatigued dog, sleep does not occur. The possibility that fatigue interferes with the 'chemical mechanism for the transmission of nerve impulses' was not ruled out by the authors' study of the acetylcholine mechanism, but acetylcholine could not be detected in the cerebrospinal fluid of normal or fatigued dogs.

Schnedorf, J. G., and Ivy, A. C. (1939) *Amer. J. Physiol.*, **125**, 491.

Treatment

Insulin

G. W. Robinson, Jnr., investigated the physiological aspect of sleep with particular emphasis on the necessity of securing complete muscular relaxation. The author quotes Wegierko in saying that relief from pain has been obtained in certain conditions by the institution of mild insulin shock, and that such relief apparently came from relaxation of muscular spasm. Applying this to the problem of securing rest, it was found that insulin injections combined with a high carbohydrate intake had a definitely sedative effect. The essentials for a perfect hypnotic were an optimal degree of relaxation, little subjective sensation, and lack of after-effects. Insulin was considered highly effective when used in psychiatric hospital practice for such cases as mania, over-activity, and hysteria, and especially in post-alcoholic insomnia. Dosage and routine were varied to meet individual needs.

Robinson, G. W., Jnr (1939) *Clin. Med Surg.*, **46**, 61.

INTESTINAL OBSTRUCTION

See also Vol. VII, p. 221, and Cumulative Supplement, Key Nos. 761–775.

Intussusception

C. P. G. Wakeley and F. R. B. Atkinson analysed 121 cases of intussusception under the care of the first-named. The condition was much commoner in males, being 70 per cent, thus practically agreeing with 68 per cent in Fitzwilliams' 1,000 collected cases (1908), and 64 per cent in the 400 cases analysed by W. S. Perrin and E. C. Lindsay (1921) at the London Hospital. The largest number of cases occurred in the first year of life, namely 72 (50 males), the youngest being in a female aged 3 weeks, and the oldest, a male 8 years old. Analysis of the cases occurring during the first year of life showed that the highest incidence was in the 7th month; this was ascribed to the presence of enlarged glands in the root of the mesentery and the ileocaecal angle together with a preponderance of lymphoid tissue in the terminal ileum and around the orifice of the ileocaecal valve, the change in the wall of the ileum acting as a foreign body and causing increased and irregular peristalsis. The first-born child was attacked in 77 out of the 121 cases. In 67 cases the intussusception was ileocaecal, and in 41 ileocolic. The 4 commonest symptoms were abdominal pain, often sudden in onset and intense, vomiting, and later blood and mucus in the stools (80 per cent) and an abdominal tumour (50 per cent). Death followed operation in 12 cases.

Treatment

Barium enemas.—J. M. Nordentoft advocated the use of barium sulphate enemas combined with radiography in the examination and conservative treatment of intussusception in infants and children. It thus served a double purpose. After a summary of the history of this method, he showed, on the basis of 440 cases collected from the Danish publications during the years 1928–35, the increasing use of barium

enema reduction. Nearly all forms of intussusception involving the colon (colic and ileocaecal) in children could be thus reduced if the method was carried out within the first 24 hours of the onset. In cases in which operation was necessary, it helped the surgeon by moving the invagination from the left to the right, thus enabling him to confine the incision to a small size on the right side, and by making a deep invagination less deep. Barium enema and fluoroscopy also render possible the diagnosis of an irreducible ileocolic invagination, preventing needless conservative attempts at reduction. Rupture of the intestine from the barium enema was only a theoretical objection. The use of steady constant pressure from a column of 1 metre of barium, if combined with general anaesthesia, gave the best results; sometimes a momentary narcosis, the enema being still retained, effected reduction. A conical thick nozzle tube should be employed for the procedure, so as to prevent escape of barium sulphate from the rectum.

Fitzwilliams, D. C. L. (1908) *Lancet*, **1**, 628

Nordentoft, J. M. (1939) *Acta radiol., Stockh.*, **20**, 128

Perrin, W. S., and Lindsay, E. C. (1921) *Brit. J. Surg.*, **9**, 46

Wakeley, C. P. G., and Atkinson, I. R. B. (1938) *Brit. J. Child Dis.*, **35**, 241.

Obstruction of the Small Intestine

Polyposis

In the opinion of I. A. Shaw, the chief clinical feature of polyposis of the small intestine is the production of an intussuscepted mass, usually in the left side of the abdomen. The mass is tender, doughy, and freely mobile. It may not be constantly present, and is elongated rather than circular in shape. Nausea and vomiting increase with the rapidity and completeness of the obstruction. Peristalsis is usually visible. Distension and shock are late manifestations. The white blood cells increase rapidly as the intussusception develops, the count rising to about 20,000. These polypi can occur at any age, and may be congenital. They have a tendency to malignant degeneration. Pre-operative diagnosis is difficult, as medical advice may not be sought at an early stage. An acute abdominal crisis is usually the basis for the surgeon's first contact. The author in a series of 7 operations performed a resection twice: a side-to-side anastomosis and an end-to-end anastomosis. In the remainder the polypi were excised and the bowel was closed. To avoid the complications of obstruction and malignant degeneration, when the signs and symptoms are obscure, the author urges a more careful radiological examination of the small bowel in the routine examination of the gastro-intestinal tract.

Shaw, E. A. (1939) *New Engl. J. Med.*, **220**, 236

Malignant Disease of the Duodenum

Primary Leiomyosarcoma

A. J. Mendillo and W. B. Kaufman, who stated that primary sarcoma of the duodenum has been reported in 62 cases, reported a case of primary leiomyosarcoma of the duodenum combined with a diverticulum of the duodenum. The patient was extremely anaemic from haemorrhage due to ulceration of the duodenal surface, but recovered after excision of the tumour.

Mendillo, A. J., and Kaufman, W. B. (1938) *New Engl. J. Med.*, **215**, 432.

Duodenal Ileus

Clinical Picture

K. Mitsuba *et al.* proved in a previous paper that the stagnation of the duodenal contents and the resulting toxic manifestation were of the greatest importance in ileus, and found a positive kynurenin reaction, increasing in amount in proportion to the severity of the ileus. Kynurenin being an intermediate product between tryptophane and kynurenic acid, it was concluded that in acute ileus the function of the liver is damaged. The kynurenin reaction occurred not only in animals but also in 12 cases of acute ileus in man. Experimentally 2 factors were necessary for a positive kynurenin reaction: hepatic inadequacy and excretion of tryptophane from the body fluid, conditions present in acute ileus. The main cause of the impairment

of hepatic function was stagnation of the duodenal contents and a change in the resorptive power of the latter.

Mitsuba, K., Suehiro, S., and Itagaki, C. (1939) *Klin. Wschr.*, **18**, 284.

INTESTINES, TUBERCULOSIS

See also Vol. VII, p. 253.

Diagnosis

Triboulet's Test

H Leick reported his observation on the use of Triboulet's test which has been used since 1910 for the diagnosis of intestinal tuberculosis. An aqueous solution of the faeces is filtered, and 20 drops of a solution consisting of 100 c cm. of 3.5 per cent mercuric chloride and 1 c cm. acetic acid is added, a more or less heavy precipitate forms. The author examined the test in other conditions, and found that there was no specificity in its result, as the same results were obtained in diphtheria, mumps, pneumonia, jaundice, and other conditions.

Leick, H. (1939) *Munch. med. Wschr.*, **86**, 1020.

JAUNDICE

See also Vol. VII, p. 261, and Cumulative Supplement, Key Nos. 779-788

Catarrhal Jaundice

Aetiology

G. M. Findlay *et al.* investigated the aetiology of infective hepatitis, or epidemic catarrhal jaundice, in man, and came to the conclusion that it is a virus disease. The evidence that this is so is provided by its long incubation period, the fact that it is difficult to transmit to lower animals, and because no bacterium, spirochaete, or protozoon has been isolated which could account for it. The authors suggested that jaundice which followed the injection of an attenuated strain of the yellow-fever virus was identical with infective hepatitis, because the symptomatology and pathology of the conditions were identical, and therefore presumably the aetiology also. It was suggested that the virus is present in the serum used for inoculation, and it was advised that serum should not be taken from subjects unless they had been healthy for at least one month, i.e. for the incubation period of infective hepatitis.

Clinical Picture

F. R. Cullinan stated that the only important forms of infective jaundice in England were Weil's disease and catarrhal, or common, infective jaundice. Of these, common infective jaundice may occur epidemically or sporadically. Outbreaks start as a rule between August and March. There is a prodromal stage of malaise lasting 1 to 7 days. The appearance of jaundice usually coincides with the beginning of convalescence. A clinical test for latent jaundice is to press a glass slide over a histamine wheal, when the centre of the wheal is seen to be distinctly yellow. Spread of infection is invariably by close contact. Water, milk, and food play no part. Infectivity is only high when contact is close, for example in schools. The incubation period is between 21 and 35 days, though some authorities believe a short period of 4 days may also occur. Probably the infectious period is short, and before the onset of jaundice. The jaundice may be so fleeting that it is not diagnosed. Urinary bile-pigments are then of importance. The pathology is probably a necrotic liver-cell lesion of a very mild order, starting in the central zone of each lobule. The evidence for an obstructive catarrhal cholangitis is very dubious. It is probable that acute and subacute necrosis of the liver is often nothing more than a very severe common infective jaundice. Post-salvarsan jaundice frequently occurs in epidemics, often associated with epidemics of common infective jaundice. It is suggested that syphilis and salvarsan render patients more liable both to infection and to severe attacks. Outbreaks of apparent common infective jaundice have followed prophylactic inoculations for yellow fever and measles. It is probable that the human serum used contained the hepatotoxic virus.

Treatment

Desensitization. - F. Corelli expressed his view that a large number of cases of catarrhal jaundice are due to an allergic condition. Treating over 100 cases with a

method aiming at desensitization, 80 per cent of favourable results were obtained. The treatment was desensitization by general, non-specific means, by the injection of calcium, sodium hyposulphite, and ephetonin (synthetic ephedrine). The clinical histories confirmed the author's view that icterus catarrhalis, due to increased sensitivity and exudation, can be easily controlled by desensitization.

Corelli, F. (1939) *Polyclinico*, **45**, 1131.

Cullinan, E. R. (1939) *Proc. R. Soc. Med.*, **32**, 933.

Findlay, G. M., MacCallum, F. O., and Murgatroyd, F. (1939) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 575.

Spirochaetosis Icterohaemorrhagica

Clinical Picture

W. Esmond Rees recorded 6 cases of spirochaetosis icterohaemorrhagica (Weil's disease) in the South Wales coal-field, the first to be recorded in that area. Three of the patients worked in the same part of the same pit, and 2 other men in a colliery at some distance. All the men worked in very wet pits infested with rats. The clinical diagnosis, which was made from the combination of jaundice and nephritis, was confirmed by laboratory tests described in an accompanying paper by A. F. Sladden. One of the 6 patients died, and another death occurred in the area, but the case was not included in this report. The degree of jaundice varied. Among haemorrhagic manifestations, epistaxis and labial herpes were the most common; in one instance corneal involvement left some impairment of vision. A positive Wassermann reaction was present in the cerebrospinal fluid in 2 cases, and subsequently became negative on recovery. An observation not reported in previous outbreaks was monocytosis in the blood.

Diagnosis

Appearance of conjunctivae.—K. M. Robertson thinks that the appearance of the eyes is a valuable diagnostic physical sign in spirochaetosis icterohaemorrhagica (Weil's disease). The whole of the bulbar conjunctiva appears inflamed, but there is less 'anger' than in an inflammatory conjunctivitis and in the injection seen in measles, and the slight conjunctival oedema imparts to the whole a watery look. The colour is more pink than red. This appearance is evident within 24 hours of the onset, and may persist until the jaundice shows. The intramuscular injection of serum on 3 or 4 successive days in doses up to 40 c.cm. daily, even before the agglutinin test has been returned positive, is strongly advised. A high-carbohydrate protein-free fluid diet is an ideal adjuvant.

Rees, W. E. (1939) *Brit. med. J.*, **1**, 603.

Robertson, K. M. (1938) *Brit. med. J.*, **2**, 1300.

Complications of Operation

Haemorrhage

C. F. W. Illingworth finds that post-operative haemorrhage in jaundice is a comparatively common cause of severe complications, and quotes Fraser's figures to show that the ensuing mortality may be as much as 12 per cent. He thinks that the main factor in this may be deficient blood-coagulability, which is associated with a fall in the prothrombin level below a certain figure. This fall is greater in obstructive than in toxic jaundice, and is most marked in long-standing deep jaundice. An estimation of the prothrombin may be of assistance in calculating the liability to haemorrhage. The administration of vitamin K has considerable effect in counteracting this liability, but it must be continued throughout the post-operative phase. Care must be taken to avoid the formation of an external biliary fistula.

Illingworth, C. F. W. (1939) *Lancet*, **1**, 1031.

JOINTS, DISEASES AND DISORDERS

See also Vol. VII, p. 278.

Pulmonary Osteoarthropathy

Chronic hypertrophic osteoarthropathy, as its full title, hypertrophic pulmonary osteoarthropathy, implied when described in 1890 by Pierre Marie, is usually



A



B

A Tuberculosis of right hip-joint in female, aged 22. Skiagram taken before operation. Note calcified debris above neck of femur and in region of great trochanter. B Same patient skiagram taken after operation (intra- and extra-articular arthrodesis) shows the graft as a firm boss of bone extending from the ilium to the great trochanter. (From *The British Journal of Tuberculosis*, 1939)

PLATE III

[To face p. 391]

associated with intrathoracic disease, especially bronchiectasis and chronic empyema. In some otherwise typical cases there is no evidence of a primary infective focus. Such a case was reported by D. C. Campbell *et al.* who refer to an unpublished collection of 156 cases made at the Mayo Clinic by Stephens (1928) with 14 per cent of such anomalous cases. Their case resembled the few recorded examples of familial acromegaloïd-like skeletal disease (Müller) or idiopathic familial generalized osteophytosis (Freund). Lesions of the joints occur in about one-third of all the reported cases. Although the disease has been recorded as arising spontaneously in animals, attempts to produce it experimentally have failed.

Campbell, D. C., Sacasa, C. F., and Camp, J. D. (1938) *Proc. Mayo Clin.*, **13**, 708.

Freund, E. (1938) *Amer. J. Roentgenol.*, **39**, 216.

Müller, W. (1930) *Beitr. klin. Chir.*, **150**, 616.

Tuberculous Hip

Treatment

Arthrodesis.—E. H. Allon Pask stated that arthrodesis was indicated in tuberculous disease of the hip-joint (i) in old-standing cases in which the deformity progresses; (ii) in those in which the disease has recurred after conservative treatment, time being allowed for the condition to subside before operation is performed; and (iii) for persistent chronic pain in an otherwise quiescent joint. Stress was laid on the importance of avoiding operation when the disease is active. The author reported 11 cases in which operation was undertaken, combined intra- and extra-articular arthrodesis being carried out whenever possible (see Plate III). In every case the graft was taken from the anterior part of the ilium. Firm bony ankylosis in good position was obtained in 10 cases. The operation is not justifiable in young children.

Pask, E. H. A. (1939) *Brit. J. Tuberc.*, **33**, 42.

Tuberculous Knee

Treatment

Surgical.—E. Ducrey describes the surgical treatment of tuberculosis of the knee-joint. There is a preparatory treatment consisting of resting the joint in a plaster cast fixed at the back of the joint to allow for air and sun-ray treatment. If, after some months, the acute inflammation has been rendered inactive, the joint is resected and, after 5 to 6 months of air and sun-ray treatment, the patient is allowed to walk with a plaster-of-Paris cast, and later with a celluloid splint. The latter must be worn for another year. The advantages of resection are that all tuberculous foci are eliminated, that the patient will have, after 5 or 6 months, a knee which is strong, ankylosed, and usable, and that much money and nervous strain are saved as compared with the conservative treatment which takes years. The author limits the surgical treatment to adults. He cites Sorel who recommends no resection in children, resection in adults, and amputation in old people. Another very important point is not to resect before the joint is in the inactive stage. The author uses the classic intra-articular type of resection. The knee-joint is opened when in slight flexion, and a metallic protector is fixed at the popliteal space to prevent injuring any blood vessels. The resection is executed with a double saw after the method of Calvé-Galland. The limb is then fixed in a plaster cast, also according to the Calvé-Galland method, with a metallic mechanism which allows prolongation or shortening of the whole apparatus.

Ducrey, E. (1939) *Dtsch. Z. Chir.*, **251**, 491.

Hip-Joint

Osteoarthritis

Osteotomy.—According to H. J. Seddon, when osteotomy is performed for correction of deformity in an ankylosed hip, it is often possible to compensate for moderate true shortening by fixing the hip in abduction. The required angle may readily be determined if the true shortening and the distances between the femoral heads are known. The second measure is best obtained by radiography, though allowances must be made for magnification of the image produced by an X-ray

tube at a distance of less than 6 feet from the patient. Tables to calculate the magnification with the tube at 30 inches and at 6 feet are given.

Seddon, H. J. (1938) *Lancet*, **2**, 552.

Habitual Dislocation of Patella

P Pitzen states that there are a great many causes for habitual dislocation of the patella. Changes in each part of the knee-joint may cause this condition. In most of his cases in which the dislocation was congenital the author found a 'patella alta', i.e. a patella which rested too high up. He distinguishes 2 types of patella alta; a patella alta vera in which the ligamentum patellae proprium is too long and in which the patella is too central in position, and a patella alta spuria in which there is a pathological turning away of the condyles. His operative method for dealing with either type of patella alta is quite simple. He incises the skin in order to expose the ligamentum patellae proprium. One or 2 thick silk threads are passed through the medial border of the ligament, and are carried subcutaneously around the patella and through the lateral border of the ligament. It is quite easy to direct the patella to a proper position by means of the silk 'reins'. The leg is extended, the wound closed, and the leg kept in a plaster-of-Paris bandage for about 5 or 6 weeks. The author treated 6 patients successfully by this method.

Pitzen, P. (1938) *Munch med Wschh*, **85**, 1577.

Use of Cellophane in Arthroplasties

T Wheeldon has used Cellophane for the lining of joints in arthroplasties in nearly 50 cases. He has operated on hips, knees, shoulders, wrists, and fingers, the result being excellent function in the joints and no irritation either post-operatively or subsequently. He believes that Cellophane remains unabsorbed indefinitely. He used No. 300 moisture-proof transparent film, 0.00088 of an inch thick. If this is boiled for 20 minutes, the only change in it is in the direction of increased toughness. He reported a case of repair of the tendon of the extensor pollicis longus, 4 weeks after injury, by the use of Cellophane as a permanent tendon sheath. The ends of the tendon were found to be 5 inches apart, and this gap was bridged by a tube of Cellophane which was sutured with plain catgut to the torn ends of the tendon. The wound healed by first intention, and there were no signs of irritation. The operation was followed by massage and movements, and the patient now has excellent extension of his thumb, and there is so little contraction of the extensor pollicis longus that he can flex it almost normally.

Wheeldon, T. (1939) *J Bone Jt Surg*, **21**, 393.

JOINTS, INJURIES AND INTERNAL DERANGEMENTS

See also Vol VII, p. 321.

Cysts of External Semilunar Cartilage

Actiology

Writing on cysts of the external semilunar cartilage S. Kleinberg, who quotes the collection of 163 cases by Bennett and Shaw, pointed out that the cysts are generally formed by the coalescence of small cysts and contested the view that trauma and a resulting haematoma are responsible, pointing out that these originally multilocular cysts are not seen after rupture and displacement of the semilunar cartilages.

Kleinberg, S. (1938) *Arch Surg*, **37**, 827.

A Method of Joint Measurement

F. J. Wiechec and F. H. Krusen stressed the necessity for an accurate and standardized method of measuring joint movement. In addition to the aid which it affords the physician, the psychological effect of joint measurement on the patient in interesting him in his rate of progress is of considerable value. It is also the objective test of disablement, and is essential for medico-legal work. Several different methods and recording instruments are described, the uses of which are limited by their wide variations in nomenclature and the starting point from which measurement should be calculated. A new system is presented which defines the movements

of nearly all the joints of the body, and an instrument is described that will measure joint motion accurately. Approximately normal ranges of movement are also given.

Wiechec, F. J., and Krusen, F. H. (1939) *Amer. J. Surg.*, **43**, 659.

KIDNEY, SURGICAL DISEASES

See also Vol. VII, p. 380, and Cumulative Supplement, Key Nos. 829-840

Congenital Abnormalities

According to H. von Jaschke congenital malformation of the kidneys are much commoner than is generally realized. Statistics of necropsies show that they occur in about 1 per cent of all bodies. The author reported 2 cases, the first of a man with a right renal calculus and anuria in whom post-mortem examination after nephrolithotomy showed that the left kidney was absent. The second patient was a woman with a right renal calculus and anuria. No left ureteric ostium could be found. Anuria might occur in cases of renal calculus as the result of reflex anuria of the unaffected kidney. In the above patients there were attacks of intermittent anuria.

Jaschke, H. von (1939) *Deutsch. med. Wschr.*, **65**, 163.

Calculi

Morbid Anatomy

Renal lipomatosis, or hyperplasia of the fat around the renal pelvis, has been found in all cases of long-standing calculous disease of the renal pelvis. Some degree of increase of fat occurs in chronic renal tuberculosis and pyonephrosis but not in acute infections, such as pyelonephritis and abscess, chronic Bright's disease, renal tumours, or hydronephrosis of the pelvic type. C. E. Dukes, from whom the above details are taken, considers that this is an advantage as the increased amount of fat, due to stimulation by the calculus, acts as a cushion or buffer, like a packing of cotton-wool, and minimizes injury and friction.

Chemical Composition

M. Ratner and A. Strasberg recorded a case in an obese woman, aged 48, who passed 2 large and 25 small calculi. Chemical analysis of the large calculi showed that they contained 60 per cent of xanthine, 30 per cent of uric acid, and 10 per cent of calcium oxalate. The calculi were yellowish, with brown streaks, smooth and radio-opaque, contrary to the usual finding and probably due to the calcium. Xanthine calculi are very rarely recognized, and this is only the seventeenth discovered since the condition was first described by Marcet in 1817, as 6 only have been reported since 1901, their incidence and recognition have not been influenced by radiography and pyelography.

Dukes, C. E. (1938) *Proc. R. Soc. Med.*, **31**, 1361.

Ratner, M., and Strasberg, A. (1939) *Canad. med. Ass. J.*, **40**, 35.

Tumours

Clinical Picture

Associated arterial hypertension. The general impression is that primary renal growths are not accompanied by arterial hypertension. Volhard recorded hypertension in hypernephroma and a fall of blood pressure after removal. Morlock and Morton, however, from analysis of 335 cases of hypernephroma, concluded that hypertension is not more frequent in this condition than in normal persons, and that removal of the tumour is not followed by a fall of the blood pressure. M. C. Pincoff and J. E. Bradley, who quoted the above observations, reported 4 cases of Wilms's embryonal adenosarcoma in which the blood pressure was raised, and in 2 of these fell after removal of the growth, but went up again with recurrence of the growth. Three of the patients were 2 years old, and the other was 2 months of age. As hypertension is very rare at these ages, their observations militate against the suggestion that hypertension was accidental and independent of the Wilms's tumour, and support the view of a renal hypertension, as in polycystic disease of the kidneys.

Wilms's Embryoma

R. O. Stern and G. H. Newns analysed 26 cases of Wilms's embryoma of the kidney. The growths were commoner on the left than on the right side, and visceral metastases

were uncommon. Nephrectomy was performed on 16 patients, 4 of whom are still alive. It was suggested that the prognosis is more hopeful if nephrectomy is preceded by deep X-ray therapy.

Pincoffs, M. C., and Bradley, J. E. (1937) *Trans. Ass. Amer. Phys.*, **52**, 320.

Stern, R. O., and Newns, G. H. (1938) *Arch. Dis. Childh.*, **13**, 193

Renal Cysts

Four unusual types of renal cyst were presented by J. A. H. Magoun. In the first case a left nephrectomy was performed, and a cyst was found in the lower third, involving the cortex and medulla and containing clear straw-coloured fluid. The cyst almost completely occluded the renal pelvis. The enlargement of this cyst occurred within a month, as shown by pyelograms, and the middle calyx became obliterated by this rapid advance. Diagnosis of a papillary tumour of the renal pelvis was made. The second case exhibited an intrapelvic tumour of unusual size, the diameter measuring 6 cm. A smaller cyst was also present containing several small calculi and grey purulent matter. An irregular growth had infiltrated the pelvis and parenchyma of the kidney. Adenocarcinoma was diagnosed. In the third case almost the entire kidney had been invaded and obliterated by a neoplasm. Compression of intrarenal drainage pathways had resulted, with consequent formation of cysts, similar to simple serous cysts. Again, adenocarcinoma was diagnosed. The fourth case was of particular interest because it showed the presence of a neoplasm and a haemorrhagic cyst, entirely separated, and with no evidence of growth in the cyst wall. It was assumed that, after the cyst had formed, the wall became calcified, and the neoplasm arose entirely from outside the cyst wall.

Magoun, J. A. H. (1939) *J. Urol.*, **41**, 831

'Hydrocele Renis'

The term 'hydrocele renis' is applied to a condition in which the kidney is partially or wholly surrounded by fluid, which may lie immediately on the kidney and be enclosed by the two layers of the renal capsule, or may be enclosed between them. The contents of the sac may be urinous, serous, or sero-sanguineous. Only a few cases have been described in the literature. S. R. Woodruff and H. S. Rupert consider that the causal factors might be renal trauma, peri-renal inflammation, or lymphatic or urinary obstruction. Symptoms include a sense of fullness accompanied by a palpable abdominal mass, varying in size and consistency according to the fluid tension present. Secondary symptoms result from compression of the organs by the mass. Pyelography eliminates the presence of cysts elsewhere, but the final diagnosis may possibly not be made until operation, as differentiation between a solitary cyst and hydrocele renis is extremely difficult. An epithelial cell-layer is present in the sac lining of the former condition, but absent in the latter. Hydrocele renis may be strongly suspected with a history of trauma, an abdominal mass, and a dislocated, compressed ureter. The only relation between hydronephrosis and hydrocele renis is that increased intrarenal pressure may be a factor in the causation of either or both conditions. Treatment is surgical, the authors advising a 2-stage operation, consisting of puncture of the sac and gradual withdrawal of fluid, followed later by nephrectomy.

Woodruff, S. R., and Rupert, H. S. (1939) *J. Urol.*, **41**, 919

LABOUR: OBSTRUCTIONS IN THE SOFT PASSAGES

See also Vol. VII, p. 511.

Obstructions due to Hydatid Cyst

M. P. Embrey recorded 2 cases of obstructed labour due to a pelvic hydatid cyst, the only examples of this rare condition seen at the Royal Cardiff Infirmary in 15 years; both of these were examples of secondary echinococcosis with multiple cysts in the peritoneal cavity. In neither case was there a history of anaphylactic manifestations such as may accompany the rupture of a primary cyst, namely, urticaria, dyspnoea, cyanosis, abdominal pain, vomiting, syncope, and delirium.

Embrey, M. P. (1938) *Brit. med. J.*, **2**, 1201

LABOUR: COMPLICATIONS OF THE THIRD STAGE

See also Vol. VII, p. 523.

Use of Posterior Pituitary Extract

B. L. W. Williams studied the effect of the intramuscular injection of 5 units of posterior lobe pituitary extract given immediately after the birth of the child in 50 normal primiparae. Fifty control cases were also investigated. In the treated series one case of contraction ring and 5 cases of post-partum haemorrhage were encountered. Among the controls there was no instance of a contraction ring, and only 2 post-partum haemorrhages. The average duration of the third stage was 8.3 minutes in the treated series, but 13.5 minutes in the controls.

R. C. Percival also compared the relative results obtained in 69 cases of labour from injecting 5 units of pituitrin (pituitary extract) immediately after the birth of the child with those in 74 untreated controls. In this series there were no cases of contraction ring, pituitary shock, or chorion retention in the treated series. The duration of the third stage was not appreciably affected by the injection, though the average blood-loss and the incidence of post-partum haemorrhages were less.

Percival, R. C. (1939) *Proc. R. Soc. Med.*, **32**, 923

Williams, B. L. W. (1939) *Proc. R. Soc. Med.*, **32**, 920.

Obstetric Shock

Treatment

Acacia solution—L. M. Randall and A. B. Hunt reported on the use of acacia solutions in obstetric practice in cases in which there is a decrease in the volume of circulating blood as evidenced by shock and haemorrhage. The institution of blood banks and the perfection of the technique of blood transfusion has replaced the intravenous anti-shock therapy of former days, but, in rural areas for instance, there is an unavoidable delay in securing blood for transfusion purposes. Therefore, it is well to remember that saline solutions of acacia intravenously are adequate temporarily to combat shock and haemorrhage. The authors observed 93 patients who each received an average of 500 c.cm. of such solutions intravenously. A 6 per cent saline-acacia solution should be in the armoury of every country practitioner called upon to control shock and haemorrhage.

Randall, L. M., and Hunt, A. B. (1939) *Amer. J. Obstet. Gynaec.*, **37**, 819

LABOUR: OPERATIVE AND MANIPULATIVE PROCEDURES

See also Vol. VII, p. 533.

Induction of Labour

Use of Posterior Pituitary Extract

From a comparative investigation of more than 1,000 cases given pituitary extract with a rather larger number of controls, undertaken to ascertain the results of administration of pituitary extract in the third stage of labour, G. W. Blomfield concluded that there was not any danger in giving 1 c.cm. (10 units) of posterior pituitary extract or, in toxæmic cases, 1 c.cm. of pitocin. The amount of haemorrhage was not much affected, but there was on the whole a tendency to a smaller post-partum loss in the series given pituitary extract. There should not be any diminution in control of the fundus or in general care in the patients receiving an oxytocic drug, and pituitary extract should not be given as a routine in all cases.

Blomfield, G. W. (1938) *Brit. med. J.*, **2**, 1083.

Caesarean Section

Healing of Uterine Scar

O. H. Schwarz *et al.* maintain that healing of the incision of Caesarean section took place by regeneration of the muscular fibres rather than by the formation of a cicatrix, in sections of both the lower and upper segments. They found that scars

in rabbits' uteri healed by proliferation, along the line of incision, of fibroblasts which entered the spaces between the adjacent muscle bundles. The newly-formed connective-tissue shrank and came to approximate the amount normally present between the muscle bundles in the uterus; hence the scar became imperceptible. The authors believed that the same process took place in the human uterus.

Complications

W. H. Rubovits *et al* noticed that the escape of meconium into the peritoneal cavity of the mother during Caesarean section sometimes resulted in peritonitis of varying severity, in adhesions, or in delayed healing of the uterine and abdominal wound. They therefore investigated the pathogenic properties of meconium, and found that it had a low-grade toxicity, and resembled bile in its pathogenic properties, though it produced a more severe local inflammatory reaction than bile.

R. Mitchell draws attention to the tremendous improvement in the mortality of Caesarean section from the beginning of the century, and considers that this is due to the introduction of antiseptic surgery and to Sanger's insistence on the necessity for suturing the uterus. The extremes of present-day views are discussed, from that of Hirsch who stated in 1928 'to-day it is safer for a woman to be delivered by abdominal section than by the vagina' to Munro Kerr who thinks that the operation should be made notifiable, and Stander who considers that the percentage of Caesarean section should not range above 4 per cent in clinics and 1 per cent in private practice. Newell gives the absolute pelvic indication for Caesarean section as a true conjugate diameter of 2 inches (5 cm) or less. Munro Kerr is less exacting, giving the true conjugate diameter as 3½ inches (8.7 cm), but the author points out that disproportion, a comfortably vague term, is frequently the sole indication stated as the reason for operation. A previous Caesarean section, although adding to the risk through possibility of rupture of the uterine scar, need not necessarily imply that, in the event of a further pregnancy, operative measures must be employed. With regard to age, a distinction is drawn between women who marry late in life and soon become pregnant and who would usually be treated as younger primigravidae, and those who have been married for years without becoming pregnant, in which cases uterine hypoplasia may be present. These deserve individual and careful consideration. Bourne points out that the mortality of Caesarean section may rise to 20 per cent in some obstetrical emergencies. He recapitulates that the low type of operation, as opposed to the classical, is to be advocated in all cases except where speed is essential and the patient not infected.

Mitchell, R. (1938) *Canad. med. Ass. J.*, **39**, 527

Rubovits, W. H., Taft, L., and Neuwelt, F. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 501

Schwarz, O. H., Paddock, R., and Bortnick, A. R. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 962

LABOUR. ANALGESIA AND ANALGESIA

See also Vol VII, p. 573

Disadvantages

Cerebral Symptoms due to Anoxaemia

Of 500 children with cerebral symptoms, seen by F. Schreiber, approximately 70 per cent of those with a birth record available had a history of apnoea. In 155 cases there was a history of precipitate, breech, twin, or premature delivery, the other 345 were all full-term infants. The total incidence of apnoea among the 155 in the first group was 72 per cent. In the other 345 infants the incidence of apnoea in the cases with a known history was 69 per cent. The depressing effect on the respiratory centre of birth analgesics given in more than pharmacological doses bears a direct relation to the degree of apnoea. The extent of the apnoea has a direct relation to the subsequent severity of the cerebral symptoms, the latter being in direct proportion to the amount of damage sustained by the brain tissue. From this it appears that very heavy doses of analgesic drugs may be the causal factor in the production of foetal anoxaemia with resultant cerebral damage.

Schreiber, F. (1938) *J. Amer. med. Ass.*, **111**, 1263.

Pentothal and Thioethamyl

Investigations were conducted by W. Bourne and A. J. Pauly into the use of pentothal and thioethamyl in obstetrical cases. A hundred women in labour were studied, with special attention to analgesia and amnesia. Of these, 80 were primiparae and 20 multiparae. Sixty were given pentothal. In 50 of these the sodium salt was used, and in the others pentothal acid. Forty were given the sodium salt of thioethamyl. As soon as pains were established, 4 gr. of pentothal were given, followed by two more doses of 4 gr. at half-hourly intervals. In some cases this was sufficient, in others 2 or 3 gr. were given every half-hour subsequently. The initial dose of thioethamyl was 6 gr., followed by two doses of 4 gr. at half-hourly intervals and 3 gr. continued at intervals if necessary. There were no toxic effects with either drug. Labour appeared to be shortened, and it is suggested that these sulphur substances cause more rapid dilatation of the cervix during the first stage. The degree of analgesia was found to be greatest with primiparae, and better with pentothal than with thioethamyl. Amnesia was only moderate with both drugs and in multiparous women their actions were too slow for rapid labour. Injections of $\frac{1}{100}$ to $\frac{1}{1000}$ gr. of scopolamine were given in some cases, and resulted in increased amnesia.

Bourne, W., and Pauly, A. J. (1939) *Canad. med. Ass. J.*, **40**, 437.

Antipyrine

During labour, B. Gershtein administers antipyrine in a dose of 8 gr. When a second dose is administered, an interval of 4 to 8 hours intervenes. When given as a suppository, 15 gr. are given, and as an enema 15 gr. in 5 to 6 fluid drachms of warm water. In only 45 out of 180 cases was the antipyrine given twice. The women became sleepy and did not complain of pain during labour. Half an hour after the antipyrine 20 c.cm. of a 20 per cent solution of magnesium sulphate were injected intramuscularly. Of the 180 cases, 64 (35.5 per cent) had completely painless labour; in 87 (48 per cent) there was a definitely good effect; and in 18 (10 per cent) the effect was doubtful. There was no effect in 11 cases (6.2 per cent). Of the babies, 172 were born alive. The author came to the conclusion that this method of painless labour is harmless both to the mother and child, and can be used everywhere. Nephritis is the only contra-indication.

Gershtein, B. (1939) *Uch. Dvdo*, **21**, 53.

LACRIMAL APPARATUS DISEASES

See also Vol. VII, p. 592, and Cumulative Supplement, Key Nos. 909-916.

Plasmacytoma

Plasmacytoma or plasmoma is one of the rarest of the tumours found in the lacrimal gland. A full account of it is given by S. T. Parker. The names have been given to any formation, inflammatory or neoplastic, composed of the plasma cell which Waldeyer described in 1871. The origin of the plasma cell is unknown, but it has been thought to arise from lymphocytes or from fibroblasts in the endothelial lining of blood vessels. In half the cases of myelomatosis the tumours were plasmacytomatous, but plasmacytomas might occur elsewhere than in bone, and, of these extramedullary plasmacytomas, 6 had occurred on the conjunctiva, and the previous 5 recurred after removal.

Parker, S. T. (1937) *Proc. R. Soc. Med.*, **31**, 130.

Chronic Dacryocystitis*Treatment*

Cod-liver oil and zinc ointment—W. Reitsch expressed the view that surgical therapy in conditions affecting the lacrimal apparatus are not always necessary, in fact, in dacryocystitis, repeated passing of the probe has the adverse effect to that which is wanted. The author tried conservative therapy in this condition and found that the best ointment was a combination of cod-liver oil and zinc (unguentolan). The ointment is warmed and made fluid and on application it acts as a kind of chemical probe, filling out the lacrimal canal.

Surgical.—In selected cases of chronic dacryocystitis L. Guy advocated the operation of dacryocystorrhinostomy because it often relieved the epiphora and infection. The operation is usually unnecessary in children because they respond to medical treatment. It should not be undertaken if an intra-ocular operation is to be performed, as the danger of ascending infection from the nasal cavity is too great. Obstruction in the canaliculi and the nasal passages may render the operation useless. Among 54 operations by 7 surgeons there were 2 failures only, and these occurred in the first half of the series. Haemorrhage from the naso-ciliary artery, haematoma, and infection of the orbit are possible complications.

P Southgate described the method originated by O. R. Neese of dealing with chronic dacryocystitis which, apart from relieving the symptoms, aimed at restoring the function of the lacrimal apparatus. The rationale of the procedure was that of the dacryocystorrhinostomies, i.e. drainage of the lacrimal sac directly into the upper nasal cavity, but the operative technique was simpler. The area around the sac was anaesthetized by the injection of a 4 per cent novocain-adrenaline solution, and the adjacent nasal area by the application of cocaine-adrenaline on a pledget of cotton-wool. The lumen of the sac was then exposed by an incision similar to, but smaller than, that used in extirpation of the sac. A fine haemostat was then forced through the sac wall, through the lacrimal bone, and into the nasal cavity. A thin tube of either stainless steel or gold, 15 mm. long and 2 to 3 mm. in diameter, was inserted into this opening, pointing downward into the nose, the skin and sac wall being closed with sutures. The fenestrated tube with three holes in the shaft and a flange of gold solder was attached to the sac end to keep the tube in place. This tube might be left *in situ* permanently or after 2 or 3 months it might be removed through the nose under gas anaesthesia. By that time a fistula had been formed and this functioned as well as the tube. To assist in the identification of the sac when it was opened, it might be filled with methylene blue solution, or a Bowman probe might be placed in the lower canaliculus, projecting into the sac. This technique had the advantage that the tube could be removed, and any of the accepted procedures still be performed if desired.

Guy, L. (1938) *Arch. Ophthalm., N.Y.*, **20**, 954.

Reitsch, W. (1939) *Klin. Mbl. Augenheilk.*, **102**, 846.

Southgate, P. (1938) *Amer. J. Ophthalm.*, **21**, 1158.

LANDRY'S PARALYSIS

See also Vol. VII, p. 604.

Treatment

Vitamin B₁

L. V. Roberts reported a case of Landry's paralysis in a boy, aged 14 years, who recovered; when admitted to hospital a fractional test meal showed absence of free hydrochloric acid, but 3 months later free hydrochloric acid was present in more than the usual quantity. Treatment included intramuscular injections of vitamin B₁, 4 mg. daily for 10 weeks, and subsequently 3 mg. by the mouth. Until the return of free hydrochloric acid was established, the acid was given by mouth. The relation between achlorhydria and polyn neuritis was discussed in the light of recent knowledge, especially of vitamin B₁ deficiency as a causal factor in neuritis. But, as the treatment by vitamin B₁ did not appreciably hasten recovery, the suggestion was made that a deficient formation or absorption of some other neuro-trophic factor might be responsible.

Roberts, L. V. (1939) *Brit. med. J.*, **1**, 1084.

LARYNX DISEASES

See also Vol. VII, p. 612; Cumulative Supplement, Key Nos. 918-927; and p. 90 of this volume.

Operations

Tracheotomy

A patient suffering from chronic laryngeal obstruction may, after the performance of a perfectly efficient tracheotomy, take a few breaths, and collapse and die.

V. E. Negus, after biochemical investigation, explained this phenomenon. During the obstruction the alkaline reserve and carbon dioxide in the blood rise in order to stimulate the respiratory centre to make an increased effort to oxygenate the blood. When the obstruction is relieved, the blood carbon-dioxide quickly falls, but that which is fixed as bicarbonate remains stationary, and the arterial blood is so alkaline that the respiratory centre no longer receives sufficient stimulus, and the patient ceases to breathe. Negus suggested that carbon dioxide should always be near the bed during the performance of tracheotomy and for some hours afterwards if necessary. If breathing is shallow, the patient should be made to inhale the gas. Ammonium chloride could be given before operation, but this is not such a convenient procedure. Negus, giving his indications for tracheotomy, holds that any patient, with sufficient laryngeal or tracheal stenosis to cause audible stridor on exertion, should be told that he is in the danger zone. If the stridor is audible when he is resting, tracheotomy should be considered; if it is audible when he is asleep, tracheotomy is urgently required.

Total Laryngectomy

Prognosis.—L. A. Schall contested the view that total laryngectomy mutilated the patient so severely as to leave him in a pitiable condition, the lot of the voiceless man being comparable with that of the blind and deaf. The most distressing moment after the operation was when the patient came out of the anaesthetic, because then the full force of the condition was suddenly thrust upon him. The position should be fully explained to the patient before operation so that he knows exactly what to expect. The inability to feel air passing through the nose or mouth during respiration is distressing, and resulting impairment of the sense of smell robs the patient of much of the enjoyment of food. The larynx also plays an important part in swallowing, and, if the patient eats too rapidly, he may be obliged to drink in order to dislodge the food. When the patient begins to talk with an artificial larynx or an 'oesophageal' voice, other people will inevitably notice him, a fact to which he must become accustomed. Some engrossing external interest in life is very important for these patients. Laryngectomy may precipitate a psychosis, but is not more prone to do so than any other operation. Schall considered that the supposed predisposition of these patients to suicide is overrated and that they do not commit suicide more commonly than any other group of diseased persons.

Negus, V. E. (1938) *Ann. Otol., etc., St. Louis*, **47**, 608.

Schall, L. A. (1938) *Arch. Otolaryng., Chicago*, **28**, 581.

Tuberculosis of the Larynx

Treatment

Ionization—V. Cotton-Cornwall confirmed the great benefit from electrical ionization in the relief of the pain caused by laryngeal tuberculosis. The current is produced by a 45-volt dry battery, and controlled by a reducing coil and a milli-ammeter. Applications last 30 minutes each, and are repeated daily until the resulting anaesthesia lasts 24 hours. As soon as the current passes the patient notices a sensation of stricture in the neck, and at the same time an inky or coppery taste in the mouth, accompanied by increased salivation. The feeling of stricture passes off in 4 or 5 minutes, but the taste and salivation persist. The pain is usually abolished after 15 minutes. The patient is free from pain for 24 hours or more after 6 or 7 applications. This relief is maintained by occasional applications, e.g. once a week or once a fortnight.

Cotton-Cornwall, V. (1938) *Lancet*, **2**, 1109.

Laryngocele

J. Blewett gave a full account of laryngocele, defined as an air-containing cyst which arises from, and communicates with, the cavity of the larynx, or herniates into the soft tissues of the neck. Although described in 1829 by Larrey, the number of recorded cases is small, but a number of references are appended to this article. It arises from the sacculus or appendix of the laryngeal ventricle, and increased pressure, as in whooping-cough, glass-blowing, playing wind-instruments, or straining as in child-birth, may lead to its distension and expansion. When confined to the larynx it is called an internal laryngocele, and when projecting into the neck it becomes an external laryngocele, and may be palpable, mainly in front of the sternocleidomastoid muscle, it may be of variable size and either fluctuant and

reducible or of stony hardness. It may obstruct the larynx and even thus prove fatal giving rise to attacks of suffocation, coughing, and dysphagia. A case was described in a North Sea fisherman, aged 48, this was diagnosed by radiography.

Blewett, J. (1939) *Brit. J. Radiol.*, **12**, 163

LEAD POISONING

See also Vol. VII, p. 658, and Cumulative Supplement, Key No. 931

Diagnosis

L. A. Windsor-McLean examined 115 men who were subjected to varying degrees of lead hazard. Their average age was 30, and their average duration of employment in this industry was two and a half years. With the exception of one man who was considered to be suffering from lead poisoning, the cases presented only vague symptoms, not necessarily associated with lead absorption. The author is critical of the value of the test for estimating the ratio of large to small lymphocytes, and thinks that the hand-grip test is unreliable, as the patient may not be putting forth a maximal effort. A dark-field method of examining red cells for polychromasia is also described by him.

Urine Excretion of Lead

S. L. Tompsett and A. B. Anderson found that, out of 29 cases of suspected lead poisoning, 11 proved to be positive. The amounts of lead in the blood and in the excreta were determined; in 10 of the cases of lead poisoning the amount of lead in the blood was more than 100 mg. per 100 c.cm. of blood, and varied from 100 to 400 mg. A daily excretion of more than 1 mg. indicated poisoning, even if the lead in the blood was below the above level. The total daily excretion in the urine and faeces of 10 cases varied from 0.22 to 2.82 mg. and did not run parallel with the blood level. The blue line on the gums and punctate basophilia were not always present, but a level of 100 mg. of lead per 100 c.cm. of blood, or a daily excretion of more than 1 mg. of lead, proved the presence of lead intoxication.

Tompsett, S. L., and Anderson, A. B. (1939) *Lancet*, **1**, 559.

Windsor-McLean, L. A. (1938) *Med. J. Aust.*, **2**, 367.

Treatment

Magnesium Sulphate

F. Capelli treated 20 patients with chronic lead poisoning by daily intravenous injections of 10 c.cm. of a 10 per cent solution of magnesium sulphate. In most cases the results were good—as well as an increased number of erythrocytes, there was also a rise of the haemoglobin percentage; the latter, however, did not always correspond with the increased red-cell count. The amount of porphyrinuria was reduced. The effect of magnesium sulphate is twofold: (i) it mobilizes the lead, allows of its removal from the bony structures, obviating toxic influence on the bone marrow, and (ii) it facilitates the excretion of the lead, thus diminishing haemolysis.

Parathormone

G. E. Beaumont and R. Wyburn-Mason describe an unusual case of lead poisoning in which the encephalopathy, transient blindness, oliguria, and raised blood-urea, all associated with abdominal pain, can be explained by the action of lead in causing the contraction of plain muscle. The conclusions drawn from their investigation were as follows: (i) The temporary retention of nitrogen in the blood coincided with the period of oliguria and disappeared with diuresis. (ii) There was no evidence of nephritis. (iii) The temporary excess of bilirubin in the blood was probably due to haemolysis. (iv) Increased intracranial pressure was present, but there was no evidence of meningitis. (v) The decreased fragility of red cells is the opposite to what occurs in acholuric jaundice. (vi) The anaemia was temporary. The patient was first treated with 4 pints of milk in 24 hours, glucose, and calcium lactate, 30 gr., thrice daily with the idea of removing lead from the circulation to the bones. After the acute symptoms had subsided, a low-calcium diet and the intramuscular injection of 50 units of parathormone daily were commenced.

Beaumont, G. E., and Wyburn-Mason, R. (1939) *Brit. med. J.*, **1**, 150.

Capelli, F. (1938) *Med. d. Lavoro*, **29**, 43.

LEISHMANIASIS, CUTANEOUS

See also Vol. VII, p. 664, and Cumulative Supplement, Key Nos 932-934.

Oriental Sore*Treatment*

Fuchsin paint—A. Castellani and G. Amalfitano reported 3 cases of oriental sore (leishmaniasis cutanea) contracted in Africa, which were successfully treated by fuchsin paint, the formula of which was saturated alcoholic solution of basic fuchsin 10 c.cm., and 5 per cent phenol solution 100 c.cm. This was filtered and 1 g. of boric acid was added. After 2 hours 5 c.cm. of acetone were added, and after a further 2 hours 10 g. of resorcinol were added. The solution was kept in dark-coloured stoppered bottles. For two days the sores were dressed with a 1 per cent boric acid solution, and a 1 per cent resorcinol solution to remove the crusts and scales. The fuchsin was then applied to the sore twice daily and 2 c.cm. of the same solution were given intramuscularly every other day. The solution could be injected into and around the skin nodule. Every 8 or 10 days the fuchsin paint was stopped,



FIG. 16. (a) Case of oriental sore before starting fuchsin treatment, (b) same patient after three months' treatment with fuchsin (from *The Journal of Tropical Medicine and Hygiene*, 1939)

and the boric acid and resorcinol solution was applied again for one or two days. The cases were cured in from 2 or 3 months, without this treatment cure usually takes 18 to 24 months (See Fig. 16)

Castellani, A., and Amalfitano, G. (1939) *J. trop. Med. (Hyg.)*, **42**, 33.

LEPROSY

See also Vol. VII, p. 682, and Cumulative Supplement, Key No 935

Bacteriology

E. Marchoux and R. Prudhomme have brought forward evidence that the *Mycobacterium leprae* and that of rat leprosy (Stefansky's bacillus) are killed by exposure to a temperature of 60° C. for 30 minutes and by drying. This conclusion was the outcome of observations made by Prudhomme that living micro-organisms *in vacuo* have the power of reducing the colour of certain substances, especially *o*-cresol-indo-2-6-dichlorophenol, but that this cannot be induced by dead micro-organisms. Drying *in vacuo* with sulphuric acid also killed the leprosy and rat leprosy bacilli; but washings of the dried bacilli contained a substance, derived from the bacilli, which reduced the colour tests much more rapidly than did living bacteria. These observations supported the view that leprosy bacilli and those of rat leprosy are very closely allied.

Marchoux, E., and Prudhomme, R. (1938) *Bull. Acad. Méd. Paris*, **120**, 174.

Prudhomme, R. O. (1938) *Ann. Inst. Pasteur*, **61**, 512

Clinical Picture

J. Lowe, in attempting to classify the distinction between the types of leprosy among Burmese and Indians living in Burma, found that the nerve type was more prevalent in Indians, and the lepromatous type in Burmese. In Indians, severe lepromatous forms are seen chiefly in adults; in Burmese this form is common and much more severe among young children. In Indians the lepromatous form is usually diffuse and not localized; infiltration may be generalized, with no definite nodulation in any area. In the Burmese, on the other hand, the disease manifests itself chiefly in marked local lesions with little general skin involvement. Lepromatous changes often occur in lesions which were previously of a tuberculoid nature. It is concluded that the Burmese patient has much less natural resistance to leprosy than the Indian, and that treatment in the former is unlikely to give such good results. The prophylactic value of isolation is insisted on, in view of the much higher proportion of infective cases in Burma.

Coexistence with Lipomatosis

A. R. de Souza published a case of symmetrical lipomatosis affecting the extremities, both lower and upper, and the upper part of the trunk, in which multiple ulcers and abscesses developed. The histological examination revealed the coexistence of a leprosy process together with the lipomatosis. Antileprosy treatment was instrumental in improving the condition.

Lowe, J. (1938) *Indian med. Gaz.*, **73**, 591.

Souza, A. R. de (1939) *Rev. brasil. Lepiologia*, **1**, 91.

Prognosis

A. Speight classified patients treated for leprosy into 3 groups: (i) those with a low sedimentation rate which remained low throughout treatment; (ii) those with an initially-raised sedimentation rate which became lower under treatment, and (iii) those with a high sedimentation rate which remained high under treatment. Sixty patients with sedimentation-index curves conforming to all 3 groups were selected and treated with general hygienic measures and bi-weekly injections of 2 to 10 c cm. of hydnoicarpus oil with 4 per cent creosote. They were treated for over 6 months, and the majority of cases for between one and 2 years. The patients in the first 2 groups responded better than those in the third. The age in the third group was higher than in the others. Speight concluded that, if all other factors, such as general health and mental attitude, were taken into consideration, the sedimentation rate was a good guide to the prognosis and treatment. It is a better guide if it is plotted as a curve at regular monthly intervals than if only a single reading is taken, as many factors may affect a single observation.

Speight, A. (1939) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 505.

Diagnosis

Leprolin Test

J. M. M. Fernandez published his results from the subcutaneous injection of 1.5 c cm. of leprolin in the diagnosis of the lepromatous or neural type of leprosy, of lupus vulgaris, lupus erythematosus, and artificial dermatitis. His observations indicated that patients suffering from tuberculoid leprosy developed a general reaction within 24 hours, consisting of rigors, arthritic pains, and pyrexia, together with a local reaction at the site of the injection. There was also a focal reaction with erythema, and a marked congestion of the existing lesions. In lepromatous leprosy the same dose of leprolin did not produce any reaction, and in the other conditions mentioned the reaction was very mild. The author recommended this method as a clinical aid in the differential diagnosis of these conditions and also of Boeck's sarcoids.

Fernandez, J. M. M. (1939) *Rev. brasil. Lepiologia*, **1**, 85.

Treatment

Vitamin B₁

J. Schowhan and R. N. Chopra point out that about 75 per cent of the cases of leprosy in India are of the nerve type, in these the injection of cobra venom has been found effective, either when given alone or in conjunction with vitamin B₁. Further investigations should be carried out regarding the possibilities of this

treatment, but, in a series of patients treated with cobra venom, 60 to 80 per cent obtained relief from pain, formication, a feeling of 'pins and needles', and the resulting insomnia. They regained normal sensations. Various possibilities of cobra venom are discussed. It is thought that, having the power of tissue digestion, if it is made to reach the interior of the tuberculoid either by local or parenteral injections, it might help in the dissolution of such growths. Dilutions of 1 in 60,000 to 1 in 80,000 stimulate the growth of tissue-culture cells, but higher concentrations, e.g. 1 in 20,000, produce a rapid destruction of growing cells. This possibility, applied to leprous nodules, has a rational basis. It is further suggested that the analgesic effect may be due to the neutralizing action of cobra venom on an excess of acetylcholine which is probably present in the neuritic type of leprosy.

Schowhan, J., and Chopra, R. N. (1938) *Indian med. Gaz.*, **73**, 720.

LEUCORRHOEA AND OTHER NON-HAEMORRHAGIC VAGINAL DISCHARGES

See also Vol. VII, p. 710, and Cumulative Supplement, Key Nos. 937-939.

Differential Diagnosis

H. A. Poindexter reported the laboratory study for differential diagnosis of 1,975 patients suffering from infective leucorrhoea. Non-gonococcal infections were common, many being due to *Trichomonas vaginalis* or *Monilia albicans*. *Trichomonas*, monilia, and Doderlein's bacillus apparently antagonize the gonococcus *in vivo*. Sulphanilamide was effective in acute gonorrhoea but not in leucorrhoea due to *T. vaginalis*. Direct smears were made from the cervix and urethra and stained by the methylene blue and the Gram techniques. Hanging-drop preparations were made from the same fresh material by suspension in isotonic magnesium sulphate solution and 10 per cent sodium hydroxide and studied for *T. vaginalis* and *M. albicans*.

Poindexter, H. A. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 1052.

Trichomonas Vaginalis Vulvovaginitis

Treatment

Pentavalent arsenic.—Pentavalent arsenical compounds are often used in the treatment of *Trichomonas vaginalis* infections, and B. M. Kesten reported 5 cases of dermatitis resulting from their use. The drug was used in the form of a powder containing acetarsone, $7\frac{1}{2}$ gr. in 12½ gr. of the powder. A maculo-papular rash and erythema occurred in 4 cases after prolonged treatment, and in one case after short intensive treatment. In one case the powder was again applied after the rash had appeared, and this resulted in a generalized dermatitis, indistinguishable from an arsphenamine dermatitis. In the others, the lesions appeared locally, on the thighs, in the antecubital areas, and on the chin.

Silver picrate.—In vaginitis due to infection with *Trichomonas vaginalis* it is comparatively easy to give relief to the patient, but difficult to prevent the recurrence of symptoms which occur after a menstrual period. H. G. Furnell treated 15 cases successfully with silver picrate in the form of picratol, a powder containing one per cent of silver picrate. The patient was placed in the lithotomy position and the vagina thoroughly cleansed with hydrogen peroxide solution. The cervical plug of mucus was removed with absorbent cotton. The vagina was then thoroughly dried and 5 g. of picratol blown in with a vaginal insufflator. Furnell found it wise to use smaller amounts, down to 2 g., in patients with small vaginæ, as the larger amounts produced irritation. The patient then inserted a vaginal suppository containing picratol every night for 6 nights, after which she returned for another insufflation. After this, suppositories were used for a further 6 nights, by which time a cure was expected. Symptoms were alleviated within a day or two, and, in this series, there was no return of the condition after the menstrual periods.

Furnell, H. G. (1938) *Med. J. Aust.*, **2**, 284.

Kesten, B. M. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 198.

LEUKAEMIA

See also Vol VIII, p. 1, and Cumulative Supplement, Key Nos 940-955

Aetiology

W. Kempner undertook a large number of experiments on 40 cases of myelocytic and 15 cases of lymphocytic leukaemia, to determine the nature of leukaemic lymphocytes. Experiments regarding the nature of leukaemic granulocytes proved complicated and difficult. Investigations of the metabolism of leukaemic immature cells would be impossible but for the rare occurrence of a case of leukaemia in which the leucocyte count is high in comparison with the red blood-cell count, and the proportion of myeloblasts to mature white cells is so great that the metabolism of both red and mature white blood-cells can be disregarded. In 9 years the author encountered only one such case. It was concluded that morphological investigation could not decide whether leukaemic cells were malignant or benign tumour cells, or normal young tissue-cells, but that the question could be answered by studies of the metabolism of leukaemic blood-cells. Metabolism by means of glycolysis (splitting of sugar with production of lactic acid) even in the presence of air (aerobic glycolysis) is characteristic of benign tumours, and to a more marked degree of malignant tumours. In common with other workers the author concluded that leukaemic cells do not show any aerobic glycolysis. The aerobic glycolysis which occurs in more mature leucocytes was found to be a symptom of their senility. Both myeloblasts and lymphoblasts exhibit the characteristic metabolism of normal young cells, and not that of cancer cells. The diminished power of resistance to bacterial infection shown by leukaemic patients is attributed to the absence of aerobic glycolysis in immature leukaemic blood-cells.

Acute Leukaemia

J. V. Cooke made observations on patients with acute leukaemia to test an hypothesis that acute leukaemia is due to an acquired failure of the normal functions of the bone marrow, such as inactivation or destruction of one of the normal factors in haematopoiesis. Eleven children with acute leukaemia were treated by injection of extracts of bone marrow in an attempt to provide the missing maturation factors in haematopoiesis. The extracts were prepared empirically, no test for potency was available, except to determine the presence or absence of a favourable response by patients with acute leukaemia to their administration. In at least 6 cases there was an unmistakable and striking increase in granular leucocytes in the circulating blood during the treatment with extracts. The author suggested that acute leukaemia may be related to a deficiency of the physiological factors necessary for the maturation of the granular leucocytes in the marrow. Of the patients treated, 4 had more or less complete remissions of the leukaemic state, and in several others there was considerably increased maturation of the granular leucocytes.

Cooke, J. V. (1938) *J. Pediat.*, **13**, 651.

Kempner, W. (1939) *J. clin. Invest.*, **28**, 291.

Diagnosis

Retinal Changes

S. S. Gibson examined the fundi of 22 patients diagnosed as leukaemia. This diagnosis was confirmed in 9 cases at necropsy, and in 7 others by biopsy. He found that the first sign of leukaemia showing in the fundus was dilatation of the veins accompanied by a normal disc and arteries. This was followed by haemorrhages of varying severity, and perivenous infiltration of white cells forming a narrow white line on each side of the veins. Two of the cases showed oedema of the disc. The haemorrhages varied, not so much with the severity of the leukaemia as with the degree of anaemia present. The haemorrhages are typically round with white centres, though this type may not be present in the early stages. The degree may be so severe as completely to infiltrate the retina. The haemorrhages also varied with the patient's general condition, tending to become absorbed when this improved, and to recur when it became worse. In this way they were a guide to prognosis. The author suggested that the anaemia, rather than the leucocytosis, should be investigated to attempt to solve the problem of leukaemia.

Injection of Adrenaline

C. H. Behr published his experimental findings on the use of adrenaline in testing the condition of the leucopoietic system, and summarized the views expressed in the literature on this subject. The subcutaneous injection of adrenaline produces a state of irritability in the leucopoietic system which results in a reaction characteristic of the condition of the patient; it shows the tendency of the leucopoietic system to undergo lymphoid or myeloid development in the very early stages of the disease. The injection of adrenaline produces a sharp rise in leucocytes in early leukaemia, which clearly points towards lymphoid or myeloid leukaemia. Accordingly, the adrenaline test gives characteristic blood pictures in systemic blood diseases in very early stages, and in infections and haemorrhagic conditions, and its use is a valuable guide to diagnosis.

Behr, C. H. (1939) *Z klin Med*, **136**, 719

Gibson, S. S. (1938) *Arch Ophthalm*, N.Y., **20**, 364

Clinical Picture*Chronic Leukaemias*

Achlorhydria—C. I. Davis examined 20 cases of chronic leukaemia (lymphocytic and myelocytic) to determine (i) the incidence of achlorhydria; histamine gastric analysis showed that 7, or 35 per cent, of the patients were achlorhydric; (ii) the existence or occurrence of leukaemia, the combination of leukaemia and pernicious anaemia, described by Leube in 1902. Macrocytic anaemia was present in 3 cases, microcytic anaemia in 2, and smooth tongue in 8, and there was not any correlation between achlorhydria, glossitis, anaemia, and nervous signs. Potent liver extract did not influence the anaemia. These observations confirmed the general opinion that leukaemia had not any demonstrable basis, and that the name should be dropped.

Susceptibility to Infections

N. Hirschberg determined the phagocytic activity of the white cells in 20 cases of leukaemia of various types. She found that the number of mature neutrophil cells which showed phagocytic activity was greatly decreased, and further that the phagocytic activity of the individual cells was much less than normal. She concluded that this decrease of phagocytic activity is one reason why infections, as evidenced by throat lesions and positive blood-cultures, are so frequent in these diseases.

Davis, C. I. (1939) *Trans. Coll. Phys. Philad.*, 4th ser., **7**, 49.

Hirschberg, N. (1939) *Amer. J. med. Sci.*, **197**, 706

Leube, W. (1902) *Dtsch. Klinik*, **43**, 177

LICHEN

See also Vol. VIII, p. 41, and Cumulative Supplement, Key Nos. 956–960.

Lichen Planus*Differential Diagnosis*

M. I. Davis draws a distinction between the linear and the zosteriform types of lichen planus. In the former the papular elements appear as narrow lines from 1 to 2 cm. wide, which may follow the course of a nerve, vein, lymphatic vessel, or one of Voigt's lines. In the zosteriform type, the lesions form a band several centimetres wide following the course of a peripheral cutaneous nerve and its branches. The parallel between the distribution of zosteriform lichen planus and the areas of segmental nerve distribution has been observed in several classic cases. A case of zosteriform lichen planus in a 45-year-old woman is described.

Davis, M. I. (1938) *Arch. Derm. Syph.*, N.Y., **38**, 615.

Lichen Amyloidosis*Clinical Picture*

G. B. Dowling and W. Freudenthal described the second case of lichen amyloidosis shown before the Dermatological Section of the Royal Society of Medicine, the other case being recorded by A. M. H. Gray in 1934. The patient, a man aged 58,

had, 5 years before, begun to have an eruption on the legs and thighs of acuminate deeply pigmented papules. The diagnosis was made by Freudenthal by histological examination from biopsies. The special features were amorphous masses in the papillary body taking the place of the collagen tissue. The horny layer also contained small clumps of amyloid in process of elimination. The appearances were not compatible with the view that the condition was primarily lichen planus with a secondary deposit of amyloid. There was not any lymphocytic infiltration or evidence of inflammation.

Dowling, G. B., and Freudenthal, W. (1939) *Proc. R. Soc. Med.*, **32**, 1029.

Gray, A. M. H. (1934) *Proc. R. Soc. Med.*, **27**, 1462.

LIPOIDOSES, THE

See also Vol. VIII, p. 67

Gaucher's Disease

Ætiology

A. J. Aballi and K. Kato collected from the literature 17 cases of Gaucher's disease occurring in infancy. These cases may be divided into 2 types: those with neurological symptoms which appear after splenic enlargement and include retraction of the head, opisthotonos, strabismus, laryngeal spasms, and flexion of the joints, and those which lack these symptoms. The former type is most usually found in cases in which onset of the disease occurs during the first 6 months of life. In both groups the course is rapid with fatal outcome. The theory of the cause of Gaucher's disease most widely accepted is that the condition arises from an overloading of certain active elements of the reticulo-endothelial system with large quantities of kersin, which in turn accumulates because of an abnormality of lipid metabolism. In infants gross changes appear in the spleen and liver which become enormously enlarged, and in the lymph nodes and the bone marrow. The distinctive feature is the presence of Gaucher cells.

Aballi, A. J., and Kato, K. (1938) *J. Pediat.*, **13**, 364.

Schüller-Christian Syndrome

Clinical Picture

M. Esser describes a case of the Schüller-Christian syndrome in a girl 14 months old. The main symptom was a considerable swelling of some parts of the skull. The urine and sella turcica were normal. The calcium (8.3 mg. per 100 c.cm.), phosphorus (3.57 mg. per 100 c.cm.), and cholesterol (135 mg. per 100 c.cm.) contents of the blood were reduced. The author found in the blood reticular giant cells containing cocci. His deduction is that the Schüller-Christian syndrome is an infective disease with a specific reaction of the reticular cells. To increase the resistance of the reticular system he administers therefore a diet rich in lecithin and other lipoids. X-ray photographs showed an improvement of the child's condition after institution of this diet.

Esser, M. (1938) *Schweiz. med. Wschr.*, **68**, 1014.

LIVER DISEASES: LIVER FUNCTION TESTS

See also Vol. VIII, p. 87

Laevulose Tolerance Test—Modification

A new modification of the diphenylamine method of performing the laevulose tolerance test is described by Ireda K. Herbert. The dose of laevulose is 50 g. for an adult or one g. per kilo. of body weight in the case of a child. Samples of venous blood are taken before the dose of laevulose, and at an interval of half an hour, one, and two hours afterwards. In a 15 c.cm. centrifuge tube 2 c.cm. of plasma is placed and 2 c.cm. of water is added with 2 c.cm. of 10 per cent zinc sulphate solution. Add 2 c.cm. 0.5 N sodium hydroxide and shake thoroughly. Centrifuge the mixture well and filter the supernatant fluid. The yield of filtrate is 4 c.cm. In a pyrex test tube

are placed 2 c.cm. filtrate and 6 c.cm. acid-alcohol diphenylamine reagent. The standard laevulose solutions (2 c.cm. of each) are similarly treated. The tubes are placed in a boiling-water bath for 15 minutes and cooled in running water. They are diluted with alcohol up to the 10 c.cm. mark and the colours are compared colorimetrically. Standard (b) is used for comparison with the filtrates from 'fasting' plasma and (a) for the remainder.

R_s —reading of standard

R_u —reading of unknown

Plasma laevulose mg. per 100 c.cm. is given by the formulae

$R_s > 20$ when standard (a) is used;

$R_s < 5$ when standard (b) is used

The effect of 100 mg. of glucose per 100 c.cm. is equal to that of 2.4 mg. of laevulose per 100 c.cm. The results are recorded of investigations in 26 subjects with no hepatic disease. The fasting level ranges from 1.5 to 3.5 mg. per 100 c.cm. The maximal level of laevulose occurs between 30 and 60 minutes after the test dose. In a case of diabetes the rise above the initial level was 15 mg. per 100 c.cm. Of the remaining 25, only 3 showed rises above the initial level of over 11 mg. per 100 c.cm. The level 2 hours after the test dose is never greater than 6.2 mg. per 100 c.cm. The diagnostic value of the test may be limited by the existence of a large functional reserve in the liver and a normal result does not exclude hepatic disease.

Herbert, F. K. (1939) *Brit. med. J.*, **1**, 867.

Hippuric Acid Test

F. W. Lipschutz introduced an intravenous method of performing the hippuric acid liver-function test. Its advantages over the oral procedure include the fact that administration of the minimal amount only of the drug is necessary, that it may be given even if vomiting is present, and that there is a reduction in time required for collecting specimens, which are fewer in number and more concentrated. The technique used was as follows: after 12 to 14 hours' fasting the patient was made to empty the bladder, after which 20 c.cm. of a 10 per cent solution (2 g.) of sodium benzoate was injected intravenously. Two specimens were collected, at intervals of one hour, and hippuric acid determinations made. In about 70 per cent of the cases studied the percentage excretion of hippuric acid was higher when this method was employed.

Lipschutz, F. W. (1939) *Amer. J. digest Dis.*, **6**, 197.

Takata's Flocculation Test

G. Hugonot *et al.* called attention to the value of the flocculation test, introduced in 1925 by Takata, not only in the diagnosis but also in the prognosis of hepatic disease, and gave examples of cases of cirrhosis and toxic jaundice in which a grave or good prognosis was indicated before the clinical evidence pointed in that direction. A positive reaction was of grave significance. It was based on flocculation produced in morbid serums or effusions in various dilutions in saline solution.

Hugonot, G., Sohier, R., and Marchal, A. (1939) *Pr. méd.*, **47**, 745.

The Liver and Plasma Prothrombin

That the liver is concerned with the manufacture of plasma prothrombin is supported by L. D. Warner's experiments in which portions of the liver (in one group 75 per cent and in another 60 per cent) were removed from rats. In the first group a number of the animals died, and showed at necropsy massive haemorrhage into the peritoneal cavity and tissues. It was concluded that the plasma prothrombin had fallen to critical levels. There was no excessive haemorrhage when only 60 per cent of the liver was removed. In both groups the prothrombin fell to 30 or 40 per cent of normal within the first 24 hours. With the more severe operation the figure fell even below 30 per cent, and in the milder operation many animals maintained a level of 70 per cent. In the second group a maximal fall was shown in 6 hours.

Normal prothrombin levels were manifest from 10 to 21 days after operation, which corresponds with the return of the liver to normal size. Exudate formation, and consequent utilization of prothrombin, subsides long before prothrombin reaches normal levels. It is concluded that the actual loss of liver substance is mainly responsible for deficient production of prothrombin.

Warner, E. D. (1938) *J. exp. Med.*, **68**, 831.

Evaluation of Various Tests

H. Shay and P. Hieman discuss fully the various tests used in the differential diagnosis of toxic and obstructive jaundice. The tests under review consist of galactose tolerance, plasma phosphatase, cholesterol partition, and glucose tolerance. The authors think that the value of the last-named has to be established by further investigation. It is suggested that these tests should be used as a group and repeated approximately 3 times a week during an attack of jaundice. In the cholesterol-partition test performed for uncomplicated obstructive jaundice, the expected result is hypercholesterolaemia with the preservation of a normal cholesterol ester ratio of 50 per cent to 70 per cent of the total cholesterol. In toxic hepatitis, typically the total blood cholesterol is normal or moderately increased with a decrease in esters resulting in a lowered ratio. Here a divergence between the intensity of the jaundice and the concentration of blood cholesterol is the rule. The authors state that in their opinion the most reliable single laboratory test in the differentiation of toxic and obstructive jaundice remains the simple galactose tolerance test, provided that it is performed early in the course of the condition.

Shay, H., and Hieman, P. (1938) *Amer. J. digest Dis.*, **5**, 597.

LIVER DISEASES: CHRONIC VENOUS ENGORGEMENT

See also Vol. VIII, p. 98.

Morbid Anatomy

E. W. Boland and F. A. Willius analysed 75 cases of cardiac disease with prolonged single or multiple episodes of congestive heart failure, in order to determine (i) the usual histopathological changes in the liver, and (ii) whether or not hepatic cirrhosis occurs; and (iii) also to correlate the clinical and pathological findings in the so-called cardiac cirrhosis of the liver if such a condition exists in order to aid in its recognition. The microscopic changes were arranged in 3 groups: (i) Atrophy of the cells in the centres of the lobules, without condensation of the reticulum or cirrhosis; among 37 cases there were 3 only with prominent necrosis of the hepatic cells. (ii) Central lobular necrosis was well marked, and condensation and thickening of the reticulum in the areas of degeneration were constant, but not genuine cirrhosis. (iii) True hepatic cirrhosis was present in 5 cases with adenomatous regeneration in 3 of them. It was concluded that, in rare instances, true cirrhosis occurs, but there are not any definite criteria whereby its presence can be recognized clinically.

Boland, E. W., and Willius, F. A. (1938) *Proc. Mayo Clin.*, **13**, 627.

LIVER DISEASES: HEPATITIS, ACUTE AND SUBACUTE

See also Vol. VIII, p. 104.

Toxic Hepatitis

The term atrophy of the liver is considered to imply degenerative hepatic changes, including cloudy swelling, and fatty degeneration, with possibly some degree of necrosis. It was found by J. F. Weir that this condition occurred in cases in which jaundice was not present. Cases are reported in which these changes were associated with disease of the gall-bladder and biliary tract, and with syphilis or the treatment thereof. The ingestion of exogenous toxins has been found responsible, as in the case quoted in which the patient developed symptoms following the administration of cinchophen for gout. Care should be exercised in the administration of any drugs which might cause hepatic damage, and patients undergoing such therapy require

regular clinical and laboratory examination. Cases in which the aetiological factors are unknown may or may not present symptoms. If present, these include nausea, constipation, and dyspepsia. The author reviewed such a group of cases, and found no trace of any known hepatic toxin. There was slight hepatic enlargement in some instances, probably caused by an underlying condition which did not become apparent, but in some patients it seemed reasonable to suppose that the attacks were acute. Recovery occurred and progress was favourable. No gross changes were observed in liver-function tests, except a tendency towards bromsulphthalein retention and some qualitative alteration in the van den Bergh test

Sulphanilamide

C. F. Garvin reports 5 cases of toxic hepatitis occurring during sulphanilamide therapy. In 4 of these, the patients had received no other drugs. Three cases of toxic hepatitis showed an associated exfoliative dermatitis, and in one the ending was fatal. In another there was recovery in spite of the simultaneous occurrence of jaundice and ascites

Garvin, C. F. (1938) *J. Amer. med. Ass.*, **111**, 2283

Weir, J. F. (1939) *Ann intern Med.*, **12**, 1845

Acute Necrosis of the Liver in the New-Born

G. Maksin reported a case of acute degeneration (necrosis) of the liver in a female who was the 3rd of otherwise normal births of a woman whose blood showed negative Wassermann and Kahn tests. On the 3rd day of life the infant refused food, and on the next day haemorrhage occurred from the umbilical stump and the vagina. The coagulation time was 11 minutes and the bleeding time more than 30 minutes. Intramuscular injections of blood were given, but the tendency to bleed continued and jaundice becoming progressively deeper led to death on the 8th day of life. Necropsy showed that there was not any malformation of the biliary tract, and that the liver cells were acutely degenerated. No cause for the condition was found

Maksin, G. (1939) *Amer. J. Dis. Child.*, **57**, 1398.

LIVER DISEASES: HEPATITIS, CHRONIC

See also Vol. VIII, p. 118, and Cumulative Supplement, Key No. 974

Aetiology

E. M. Hall and D. A. Morgan joined the controversy regarding the alcoholic or non-alcoholic causation of cirrhosis. It was pointed out that a definite increase was found in Laennec's cirrhosis soon after the repeal of the Prohibition law. Sixty-eight cases of subacute alcoholic cirrhosis were selected for description. Enlargement of the liver occurred in all cases, with an average weight of 2,760 g., while the average weight of the spleen was 360 g., approximately double the normal. The surface of the liver was smooth or finely granular in contradistinction to the hobnail type seen in chronic cirrhosis. Jaundice was recorded in 50 per cent of the series. Of the patients, 75 per cent were chronic alcoholics, the majority having imbibed a pint or even a quart of whisky a day for periods ranging from 5 to 25 years, while some drank wine. Approximately half of the livers contained excessive amounts of fat. The authors believe that in the majority of cases it is the enlargement and fatty infiltration of the liver which constitute the first development which passes into the subacute phase of cirrhosis, and later still the small hobnail liver makes its appearance.

Hall, E. M., and Morgan, D. A. (1939) *Arch. Path.*, **27**, 672

Diagnosis and Prognosis

I. R. Jankelson and H. Baker discuss the value of infra-red photography as a means of diagnosis, particularly in relation to portal cirrhosis of the liver, in which the superficial abdominal veins are shown as an enlarged network, sometimes dark and tortuous with many anastomoses. The technique employed is as follows: the abdomen is uncovered, with the patient erect or recumbent. Two rodalites with lamps of 500 watts each are placed one on each side of the patient at a distance of 3 feet. An Eastman clinical camera, equipped with an astigmatic lens over which is placed a No. 25A Wratten filter, is provided. Exposure time is one second. There

must be no movement or breathing while the photograph is taken. The improved plates are loaded and developed in complete darkness. They should be stored in an ice-box or refrigerator. This method is also of considerable value in presenting a differential diagnosis between this condition and metastatic carcinoma of the liver, diffuse abdominal carcinomatosis, and gumma of the liver, which do not customarily show an increase in the superficial veins as demonstrated by infra-red photographs.

Vitamin A in Blood

A. Chevallier *et al* expressed the view that the level of vitamin A in the blood can give valuable aid in determining the prognosis, and even help the diagnosis, in hepatic disease, mostly in cirrhosis. The investigations carried out after theoretical consideration of the problem showed that, in cirrhosis in which the blood vitamin-A level was very low or practically absent, the prognosis was very grave. In cases, however, in which the vitamin level became raised, however slightly, clinical improvement usually followed. With regard to diagnosis, the low vitamin-A level was found to be fairly characteristic of liver disease.

Chevallier, A. Olmer, J., and Vague, J. (1939) *Bull. Soc. méd. Hôp. Paris*, **55**, 928

Jankelson, I. R., and Baker, H. (1938) *Amer. J. digest. Dis.*, **5**, 414

Obstructive Biliary Cirrhosis

W. R. Gibson and H. E. Robertson, in a paper entitled 'So-called biliary cirrhosis', considered cirrhosis of the liver to be due to obstruction of the extra-hepatic bile-ducts, and not Hanot's chronic hypertrophic biliary cirrhosis. Among 8,986 necropsies at the Mayo Clinic in the years 1922-38 there were 244 cases, or 2.7 per cent, with biliary obstruction of all kinds. Of these 244 cases of biliary obstruction and obstructive jaundice there were 21, or 8.7 per cent, cases of true hepatic cirrhosis, 14 being females and 7 males, in 10 of the 21 cases the biliary obstruction was due to post-operative stricture of the common bile-duct. In 15 of the 21 cases the obstructive jaundice was intermittent. It was suggested that for these cases the name 'biliary cirrhosis' should be discarded in favour of 'cirrhosis from biliary obstruction'.

Gibson, W. R., and Robertson, H. E. (1939) *Arch. Path.*, **28**, 37

LIVER DISEASES: INFANTILE HEPATIC CIRRHOSIS

See also Vol VIII, p. 132.

Types

P. R. Evans reported 4 cases of different forms of hepatic cirrhosis in children, reviewed the subject, and concluded that there were at least 4 well-attested forms of biliary cirrhosis, namely (a) congenital biliary cirrhosis with or without congenital obliteration of the bile-ducts, (b) infantile biliary cirrhosis of Indian nurslings; (c) acquired obstructive biliary cirrhosis, and (d) acquired non-obstructive biliary cirrhosis, or Hanot's hypertrophic biliary cirrhosis. Of the first group there was a case in a baby 3 months old with congenital obliteration of the bile-ducts. In the fourth case, clinically one of portal cirrhosis, the liver was enlarged, histological examination showed unilobular cirrhosis, and the condition was regarded as hypertrophic unilobular cirrhosis. Unilobular cirrhosis was not synonymous with biliary cirrhosis.

Evans, P. R. (1939) *Arch. Dis. Childh.*, **14**, 89.

LUNG DISEASES: ABSCESS AND GANGRENE

See also Vol VIII, p. 172, and Cumulative Supplement, Key No. 987.

Clinical Picture

X-Ray Appearances

A. Garland and F. R. Berridge discuss 16 cases of suppurative pneumonitis, 11 in males and 5 in females. In 10 cases the disease was confined to the right

lung, and 7 were associated directly or indirectly with inhalation anaesthesia. In 8 the condition followed acute pneumonia, and in 10 the suppurative pneumonitis proceeded to lung abscess. Suppurative pneumonitis has 2 characteristic radiographic features: (i) homogeneous veiling of the involved portion of the lung, and (ii) increase in the lung markings. The shadowing may involve a whole lobe or only part of it. Bronchial markings are more exaggerated than vascular markings, but the increase in the latter indicates engorgement and stasis such as might be expected in any acute inflammation. If the shadowing persists, the second stage may be reached in course of time, when a cavity with a fluid level is demonstrated in the lung parenchyma. This is the absolute criterion of lung abscess formation. An intermediate stage may intervene in which a circumscribed opacity is observed amidst the shadowing, presumably the locus of a lung abscess. The cavity of a typical acute lung abscess is surrounded by a uniform opacity of density just insufficient to obscure the lung markings completely, and is usually situated towards the upper limits of the veiling. Pleural involvement is almost constant at any stage of the disease, and is shown by fluid pleural thickening or adhesions. This is to be expected in a lesion developing at the lung periphery. There is controversy as to the exact relation between acute pneumonia and pulmonary suppuration. It appears that something more than mere tissue necrosis is required to produce an abscess in acute pneumonia, and every case of suppuration must pass through a preceding stage of inflammation. Abscess cavities which are not visible on straight radiographs may be demonstrated by tomography and by lipiodol (iodized oil) introduced through the bronchoscope into the affected part of the lung. In all cases of this series conservative treatment was adopted. The authors are of the opinion that operation should only be advocated when there is radiological evidence of an abscess cavity persisting for 14 days or more. Progressive enlargement of the vomica is an absolute indication, as is deterioration in the patient's general condition. An empyema complicating any stage of the disease is always treated surgically.

Garland, A., and Berridge, F. R. (1939) *Lancet*, 1, 375

LUNG DISEASES: TUBERCULOSIS

See also Vol VIII, p. 182, Cumulative Supplement, Key No. 988; and p. 114 of this volume

Clinical Picture

Haemoptysis

A thousand cases of pulmonary tuberculosis, in 500 males and 500 females, were investigated by A. P. Ford to find out the frequency and severity of haemoptysis. It was found that males were more likely to contract the disease, but that it was more rapidly fatal in females. The risk of severe or fatal haemorrhage was twice as great in the male as in the female, but the frequency of haemoptysis was less than would be popularly supposed, occurring in only 26 per cent of the males and 18 per cent of the females. It became obvious during the course of these investigations that deaths were less frequent in the class with haemoptysis than in those without. Two reasons were advanced for this fact, firstly, that haemorrhage would most probably bring a patient under treatment earlier in the course of the disease, and secondly, the possibility that haemorrhage may wash out a cavity or promote stimulation in the blood-forming organs, so that there is an increase in blood-cells. Acute cases were much less liable to haemorrhage than chronic or subacute cases, and, contrary to what would be expected, heavy manual workers showed less tendency to haemoptysis than sedentary workers. The explanation of this fact was considered to lie in the condition of the blood-vessel walls, which, in the manual worker, would be expected to be stronger. It was not found that the menstrual cycle affected haemoptysis in any way.

Primary pulmonary tuberculosis in children—A. M. C. Macpherson has reported the results of investigation during 8 years of 850 children at the Children's Investigation Department of the Brompton Hospital for Consumption and Diseases of the Chest. Of these 850 children, shown by a positive tuberculin test to be infected with tuberculosis, the majority did not show any evidence of pulmonary lesion on ordinary clinical examination, but 202, or 24 per cent, showed opacities regarded as due to primary lesions in the lungs, because (i) there was deposition of calcium in the

lung lesions and/or in the corresponding hilum gland, and (ii) laboratory evidence of pulmonary tuberculosis, i.e. tubercle bacilli in the gastric contents, or removal of tuberculous material through the bronchoscope. None of the children had a positive sputum. Of the 202 children, 85 per cent were known to have been in contact with cases of open tuberculosis. The primary lesions were grouped as follows. (i) uncomplicated primary lesion, (a) pulmonary lesion predominating, (b) glandular lesion predominating; (ii) complications (a) resulting from hilum lymphadenitis: collapse of part of lung, bronchogenic spread of disease, and haematogenous spread of disease, (b) pleural involvement. Children shown radiologically to have a predominating lung lesion were usually 7 or 8 years old, and did not present abnormal physical signs; the deposit of calcium was sometimes delayed for as long as 2 years after the primary lung lesion was detected. Children with predominating glandular involvement were also usually free from symptoms. The complications that might occur included tuberculous broncho-pneumonia from inhalation of tuberculous material, pressure of the glands on a bronchus might cause collapse of a lobe, and this process might be repeated in another lobe after the first had expanded. This collapse was now regarded as the condition called epituberculosis which had been explained in quite another way. Frosion of the wall of a blood vessel by a caseating lymphatic gland followed by the production of miliary tuberculosis and meningitis was a grave danger for a child under one year old with a positive Mantoux test. In the 5 fatal cases from generalized tuberculosis the responsible glandular lesion was on the left side; whether this had any significance was undecided.

Cerebral Paratuberculosis

R. C. Cohen and W. Burton Wood published 5 cases of pulmonary tuberculosis with symptoms of cerebral compression and fever which ran a benign course and resolved spontaneously; the syndrome was thought to be due to exudation into the meninges of clear sterile fluid and to be allergic rather than specific. An affinity with erythema nodosum was suggested. Some authors have proposed the name cerebral paratuberculosis for this condition.

Cohen, R. C., and Wood, W. B. (1938) *Lancet*, **2**, 1344.

Ford, A. P. (1939) *Tubercle*, **20**, 378.

Macpherson, A. M. C. (1939) *Brit. J. Tuberc.*, **33**, 79.

Diagnosis

H. Harpoth and U. Gad published 9 cases of pleural perforation which show that a mixed infection of the resulting tuberculous pleural exudate does not necessarily occur. On the contrary the exudate usually remains purely tuberculous, even when the fistula is large and permanent. The diagnosis of rupture into the pleural cavity may be difficult owing to the variability and even the absence of symptoms. When there is a perforation, methylene blue injected into the pleural cavity stains the sputum. Two pressure tests, one combined with analysis of the air in the pleura, are regarded as helpful in diagnosis: in these tests the intrapleural pressure is measured after it has been raised, and also after it has been lowered by means of a pneumothorax apparatus: return to the initial pressure suggests the presence of a fistula.

Harpoth, H., and Gad, U. (1938) *Brit. J. Tuberc.*, **32**, 228.

Treatment

Thoracotomy

In a paper on 'Thoracotomy: a conservative and selective operation for the treatment of certain cases of pulmonary tuberculosis' L. O'Shaughnessy and G. Mason advocated a method of collapse therapy for cases unsuitable for ordinary artificial pneumothorax and phrenic paralysis, and less severe than total thoracoplasty. The cases were those of fibro-cavernous disease mainly limited to a middle or lower zone of one lung. The word thoracotomy, used previously for removal of the precordial ribs, was adopted for this procedure; it consisted in selective resections of relatively small portions of ribs in the vicinity of the lesions, i.e. where relaxation of scar tissue in the underlying lung was required. The portions of ribs removed at this operation were easily accessible through direct incisions and, as little retraction was necessary, tissue trauma was reduced to a minimum. The operation was therefore specially suitable for patients in poor general condition and might, though

this was not done in the cases reported, be performed under local anaesthesia. Even if it failed in any particular case, there was nothing to preclude a subsequent thoracoplasty of the standard type. In addition to accurate radiological determination of the type, extent, and localization of the disease by the ordinary antero-posterior views, lateral, tomographic, and stereoscopic views were essential. To prevent rib regeneration of the removed rib, generally occurring so soon after this operation that it would have little chance of success, cauterization of the periosteum was performed with Zenker's solution, with 10 per cent formol, or by diathermy. It was preferable to use strips of gauze soaked in Zenker's solution placed for at least 4 minutes in the periosteal bed from which the rib has been removed. Some form of pad should be applied direct over the area concerned until such time as regeneration of the ribs was complete. The clinical and radiological picture after operation was that of progressive improvement, such as occurred in other forms of collapse therapy, the pulmonary lesions (as discernible by X-ray) disappearing as the general condition improved. As the improvement materialized the sputum diminished in quantity, became free from tubercle bacilli, and ultimately ceased.

Thoracoplasty

Results following thoracoplasty were reviewed by F. S. Dolley *et al* in the light of reports of 1,636 cases, collected from 14 clinics in the United States. Of these 640 were complete thoracoplasties which means that the excision of 8 or more rib sections was undertaken; 839 were partial thoracoplasties and in these 7 or less rib sections were removed. In the reports of the remainder of the cases the two groups were not separated. It was finally concluded that, although thoracoplasty was not invariably successful, the results obtained nevertheless furnished conclusive evidence that those patients with advanced pulmonary tuberculosis would have a much better chance of arrest than if they refused thoracoplasty. From the authors' own experience sufficient knowledge had been gained to avoid the disasters which had occurred in the past. The importance of three-stage operations; of removing sufficient ribs to facilitate collapse; of allowing a sufficient length of time to elapse between each stage; and of adequate pre-operative care had now become obvious. The additional benefit of apicolysis in some cases had been realized more fully than hitherto. Post-thoracoplastic atelectasis is among the most serious complications. One of its most frequent causes is considered to be painful inspiration. To avoid this, carbon dioxide should be given every 2 hours for the first 3 days, following each stage, together with pantopon, dilaudid, or codeine to relieve the pain, so that the patient may inhale deeply. He should be turned from side to side every 3 hours and encouraged to cough. Mediastinal pendulation was found to be the most frequent cause of heart failure. It should be remembered in this connexion that paradoxical chest motion which occurs after resection of the fourth and fifth ribs becomes much more marked after partial removal of the sixth, and a further operation is preferable to a too extensive resection in one stage. Bronchial ulceration with accompanying stenosis was considered a serious complication of pulmonary tuberculosis. Thoracoplasty was contra-indicated in these cases, unless the main bronchi were patent and draining. Acute gastric dilatation and uraemia were also recognized as a possible cause of mortality.

Of the 1,636 cases considered, 396 showed occasionally or constantly positive sputum. The reason was held to be either incomplete approximation of cavity walls or bronchial or tracheal ulceration. The question of benefits obtained by thoracoplasty was satisfactorily answered by a table of comparative results, in which it was shown that 57 per cent of those who had undergone the operation had closed cavities and negative sputum, as against 10 per cent in another series who had not; 9 per cent were improved as against 7 per cent; 13 per cent unchanged or worse as against 49 per cent, and 14 per cent dead as against 26 per cent.

Bilateral Collapse Therapy

B. P. Potter treated 152 of a series of 211 cases of pulmonary tuberculosis with bilateral artificial pneumothorax, simultaneous in 119 and alternating in 33. The pneumothorax was induced on one side, and then an average interval of 10 months (sometimes as short a time as 1 month) elapsed before the pneumothorax on the other side was induced. If the lesion was progressing in the uncollapsed lung, or if pleurisy was developing, thus preventing possible collapse, it was necessary to reduce this interval. The side of the more active lesion should be treated first. The

collapse should be confined as far as possible to the affected portions of the lungs. Other forms of bilateral collapse, such as thoracoplasty and phrenicotomy, can be combined, but Potter concluded that bilateral pneumothorax was the most effective measure. He considered that all patients with bilateral cavitation should be given the benefit of bilateral pneumothorax, as both lungs responded as well as one lung alone under similar circumstances. Of the patients in whom this procedure was successfully achieved, 79 per cent are working or ambulatory.

Relapse after Pneumothorax

S. Cold investigated the frequency of relapse following pneumothorax in 106 cases. These he divided into 2 groups, (i) mainly recent cases, i.e. previously untreated cases in which X-rays showed no particular retraction or other signs of an 'older' process; (ii) chiefly chronic cases, i.e. cases that have been under treatment previously, or have been diagnosed as tuberculous for at least one year, or in which radiology showed retraction or other signs of an 'older' process. In the first group there were 96 cases, in 83 of which the lesion was entirely unilateral. The greatest risk of relapse with extension was in the first year. Of the total of 106 cases, 72 remained inactive after an observation period of 4 years, and only one showed subsequent spread of the lesion. Early relapses appeared more frequent among patients who were still undergoing pneumothorax treatment. The author felt that in his *recent* cases no connexion could be demonstrated between the frequency of relapse and the degree of collapse. In the *chronic* cases it was suggested that relapse was more frequent in cases with adhesions, but the severing of such adhesions is not indicated in recent cases treated by pneumothorax provided that they have been sputum-negative and free from any cavity for at least one year. The significance of the relation of the duration of pneumothorax treatment to the frequency of relapse had not been established.

Artificial Pneumothorax with Chlorine Gas

One per cent chlorine was used by K. S. Ray *et al.* in a series of 74 cases in which an artificial pneumothorax was induced, and the results were compared with 71 cases treated with atmospheric air. Little difference was observed in the comparative statistics, except that chlorine appeared to arrest a larger number of cases, and its beneficial effect was noted where the lungs could be only partially collapsed by artificial pneumothorax. The percentage of complications was higher in the chlorine group. The authors had considered that chlorine might exert a germicidal effect, but, from the number of cases in which the sputum was rendered negative (55 per cent as against 60.7 per cent treated with air), this did not appear to be the case.

Lobectomy and Pneumonectomy

J. C. Jones and F. S. Dolley successfully treated 4 cases of severe pulmonary tuberculosis, 2 by lobectomy and 2 by pneumonectomy. They consider that these operations may be indicated by the failure of all other methods of treatment; when there are large haemoptyses from localized lesions; when cavities persist in spite of thoracoplasty especially if basal; in an atelectatic firmly contracted honeycombed lobe, with persistently positive sputum after thoracoplasty has been completed; and in a rare unilobar basal tuberculous cavity which does not heal after the usual collapse therapy. The authors consider that there will be more indications for this type of surgery in the future.

Formic Acid

R. Hilgermann demonstrated that formic acid had a bactericidal effect on tubercle bacilli in vitro. At normal body temperature, destruction of the acid fastness, disintegration of the bacillus, reduction in the culture area, and a diminished absorption of methylene blue took place. In vivo experiments on guinea-pigs showed arrest of the tuberculous process in 54 per cent of all cases. The animals were treated with 1 c cm. of a one-millionth dilution of 0.05 per cent formic acid, once a week. Italian reports have recorded a satisfactory result from formic acid treatment in pulmonary tuberculosis; 25 out of 30 cases were much improved by this method. The author recommended the trial use of 1 c cm. of an 0.0005 per cent solution of formic acid, once every 10 days, in the treatment of pulmonary tuberculosis.

Sodium Benzoate

C. Fossati experimented with intravenous injections of sodium benzoate, 2 to

3 g. of a 20 per cent solution having been used daily for 2 to 3 weeks. He observed that the general condition improved and that the local process showed marked improvement; in 2 cases of pneumonic involvement, the foci were resorbed very quickly and no side effects were observed. The effect on expectoration was most beneficial. Radiography and the blood picture confirmed the good effect, and the author expressed the hope of further extensive trials in order to establish this treatment of tuberculosis of the lungs.

M & B 693 in Pneumococcal Pneumonia Complicating Tuberculosis

J. H. Crawford reported the case of a man, aged 22, who, after having had pulmonary tuberculosis for 3 years, developed pneumococcal pneumonia. Though recovery from a genuine lobar pneumonia supervening on a tuberculous lesion is not infrequent, the pneumococcal condition is rare, and must be considered as of serious prognostic significance. The patient was so ill that he was not expected to live more than a few hours after the sixth day of his illness. No benefit was obtained from routine treatment, but the administration of M & B 693 (2 tablets 4-hourly with a daily total of 5 g.) brought about a dramatic recovery. Toxic effects were not observed, and in all probability higher doses could have been given with safety. The drug was continued for 5 days, a total quantity of 25 g. being administered. No increase in the activity of the tuberculous lesion resulted from the infection, and subsequent radiographic investigation showed a definite improvement in the nature and extent of the disease.

Cold, S. (1939) *Tubercle, Lond.*, **20**, 301

Crawford, J. H. (1939) *Brit med J*, **1**, 608

Dolley, F. S., Jones, J. C., and Paxton, J. R. (1939) *Amer Rev Tuberc*, **39**, 145

Fossati, C. (1939) *Riv. Pat. Clin. Tuberc*, **17**, 338.

Hilgermann, R. (1939) *Med. Klin.*, **35**, 739

Jones, J. C., and Dolley, F. S. (1939) *J. thorac. Surg.*, **8**, 351

O'Shaughnessy, I., and Mason, G. (1939) *Brit med J*, **1**, 97.

Potter, B. P. (1938) *Arch. Surg., Chicago*, **37**, 132

Ray, K. S., Sen, N. N., and Dasgupta, H. N. (1939) *Amer Rev Tuberc*, **39**, 172

LUNG DISEASES: TUMOURS

See also Vol. VIII, p. 224, Cumulative Supplement, Key Nos. 992-994; and p. 115 of this volume

Malignant Tumours of Lungs and Bronchi

Ætiology

Before the war, 1914-18, primary malignant disease of the lungs and large bronchi was regarded as extremely rare. Opinion has now completely changed, and its frequency is universally recognized. W. Boyd has put forward explanations for this altered view, about which there is no doubt; but, without denying the possibility that there may have been some real increase in the incidence of the disease, he made out a logical case for the conclusion that the change was not so much of the facts as of their interpretation. As shown by G. Schmorl, the wasting disease of miners in Schneeberg in Saxony, known for 400 years, was bronchial carcinoma. In the decade ending 1936 the lungs were, after the stomach and colon, the most frequent site of primary carcinoma at the Pathological Department at Toronto. During the period in which the frequency of primary carcinoma of the bronchi has been common knowledge, the occurrence of primary mediastinal growths has practically vanished. A popular hypothesis to explain the increased recognition of bronchial carcinoma is that it is due to tarring of the roads; but, against this assumption, it is pointed out that an increase occurred in Manitoba where there are few tarred roads, in Russia where the roads are not tarred and motor cars are rare, and in Syria where conditions have remained much as in the past. The opinions of morbid anatomists have altered; in the past primary bronchial growths were probably often called Hodgkin's disease. Further, the primary carcinoma was often regarded as one of several secondary growths in the lung. Primary bronchial carcinoma is one of the most pleomorphic of tumours and the epithelial character of the constituent cells may

be lost, and so the oat-shaped cells, now known to be characteristic of bronchial carcinoma, were regarded as lymphosarcomatous. Bronchial carcinoma has certain features which assist in its recognition: it spreads both by the lymphatics and by the blood vessels; enlargement of the supraclavicular glands, especially on the right side, is suggestive, as are the situations of metastases: in addition to involvement of lymphatic glands and the liver, the bones, adrenals, kidneys, and brain are prone to be invaded.

Diagnosis

F. G. Chandler and H. V. Morlock consider that, when intrathoracic tumours arise from the mediastinum, from the pulmonary tissue or bronchioles, or from the chest wall, and in cases in which there are secondary tumours, it is advisable, after inducing an artificial pneumothorax, to introduce a thoracoscope into the pneumothorax cavity to ascertain the exact nature, extent, and precise anatomical relations of the growth and, if possible, to remove a piece for biopsy. Fluid, either serous or haemorrhagic, may complicate the field and, though completely replaced by air, the previous deposition of fibrin may obscure landmarks and all detail. Even with fluid or blood this is not always the case and, in the absence of fluid after an artificial pneumothorax, every detail stands out with amazing clearness. As regards technique a single-cannula method with a direct vision telescope is used. Through this cannula all instruments can be inserted, including the biting forceps and a diathermy knob for the arrest of any haemorrhage. A two-cannula technique can be employed for the removal of a piece of growth for histological examination.

L. A. Hochberg and M. Federer analysed the early manifestations in 60 cases of primary carcinoma of the lung. Symptoms referable to the thorax were absent in 21.7 per cent of the cases. Epigastric distress, nausea, vomiting, pruritus, dysuria, or haemorrhoids were often the first complaint. The incidence in this group was 4 times as high in males as in females and the males were not engaged in any occupation with any aetiological significance, e.g. working with silica. Eighty-one per cent of the patients were between 45 and 65 years of age. Although there was not, on ordinary clinical examination, any pathognomonic sign or symptom, evidences suggesting carcinoma of the lung were provided by changes in the cough, in the characters of the sputum, and in the occurrence of paroxysmal dyspnoea. The most useful and important accessory methods of diagnosis were (i) bronchoscopy and examination of tissue removed, (ii) examination of the accompanying pleural effusion for the presence of cells, removal of the fluid facilitated X-ray examination of the lung; in some cases of carcinoma the effusion rapidly recurred, (iii) puncture of the lung; (iv) exploratory thoracotomy; and (v) biopsy of an accessible metastatic nodule. Eleven cases are quoted in which these methods of diagnosis were used.

Prognosis

J. J. Stein investigated malignant tumours at the thoracic inlet and pulmonary apex which were first described as 'superior pulmonary sulcus tumours'. The majority are carcinomas of the terminal bronchioles of the lung. The prognosis is very poor, the average duration of life from the onset in 12 deceased patients being only 13 months. Because of their situation in the thoracic inlet and their mode of extension to the brachial plexus and inferior cervical ganglion, surgery is not indicated. No patient in this series received any benefit from radiation therapy. Since severe pain around the shoulder and radiating down the arm on the affected side is practically the first symptom in all cases, apical tumours are commonly first diagnosed as tuberculosis, neuritis, or arthritis.

Treatment

Surgical—R. C. Brock pointed out the real danger of overlooking an obstructing malignant growth when an empyema is present. He advised an exploratory thoracotomy, when there is no mediastinal involvement. The duration of survival was 6 months from the onset of symptoms. Rogers found that, in 44 per cent of cases studied at necropsy, the first symptoms were due to metastases rather than to the primary lesion. Brock is of opinion that deep X-ray therapy relieves the more urgent and distressing symptoms in two-thirds of the cases, although it does not prolong life, the presence of much suppuration, of a lung filled with exudate, or of a large mass of growth contra-indicates its use. Subtotal lobectomy was rejected on the grounds that it does not attempt to deal with the lymphatics involved, and pneumonectomy with removal of the adjacent lymph glands was advocated. For a growth in the upper lobe, the best mode of surgical approach is anteriorly; when the lower

lobe is affected the standard postero-lateral thoracotomy enables basal adhesions to be dealt with. Rienhoff advised a two-stage procedure: (i) ligation of the pulmonary artery; and (ii) the operation on the veins and arteries. He carried this out in 12 consecutive cases without a death.

Radium.—R. C. Brock and R. J. Cann discuss the insertion of radon or radium needles in cases of bronchial carcinoma which are unsuitable for radical operation. They have treated approximately 25 patients by radium or radon, and 6 cases are selected for description. In most cases 12 seeds were used of approximately 1.0 mc. The containers, which are left in for 7 days, have an outer protective sheet of platinum 0.3 mm. in thickness. Care must be taken to avoid haemorrhage particularly on the removal of the container, and also to prevent the latter from slipping through the stenosed part of the bronchus into the dilated distal part. In 5 of the 6 cases discussed, the average survival period after treatment was 13½ months, the longest being 21 months. This compares well with the normal expectation in untreated bronchial carcinoma, which is approximately six months. Originally, the authors sought only to relieve symptoms and prolong life by unblocking an obstructed bronchus, and allowing drainage of a lung or lobe, but the results obtained lead them to believe that in certain selected cases a cure may be attempted. Radon tubes may be inserted at different stages in the bronchi on both sides, giving a cross-fire action, and allowing irradiation of the regional lymphatics, in addition to the neoplasm. The best results may be expected in slow-growing well-differentiated squamous-celled growths, often found in elderly men.

Boyd, W. (1939) *Trans. Coll. Phys. Philad.*, 4th ser., **6**, 317

Brock, R. C. (1938) *Lancet*, **2**, 1103

— and Cann, R. J. (1938) *Giv's Hosp. Rep.*, **88**, 371

Chandler, F. G., and Morlock, H. V. (1938) *Brit. med. J.*, **2**, 982

Hochberg, L. A., and Lederer, M. (1939) *Arch. intern. Med.*, **63**, 80.

Rienhoff, W. F. (1933) *Johns Hopk. Hosp. Bull.*, **53**, 390

Rogers, W. L. (1932) *Arch. intern. Med.*, **49**, 1058

Schmorl, G. (1922) *Zbl. allg. Path. path. Anat.*, **33**, 577

Stein, J. J. (1938) *J. Amer. med. Ass.*, **111**, 1612

LUNG DISEASES: POST-OPERATIVE COMPLICATIONS

See also Vol. VIII, p. 235

Pulmonary Tuberculosis

Radiological Examination

A. Gosset *et al.* advocated the systematic radiological examination of the chest before surgical operations, a precaution which 2 of the authors had taken since 1912. Accounts were given of 11 cases occurring in the Salpêtrière within a few months. This procedure might prevent acute post-operative activity of tuberculous foci in the lungs, such as occurred in 4 cases which were so urgent that pre-operative radiological examination was not carried out and ether anaesthesia was employed. In other cases radiological examination showed the presence of tuberculous lesions in the lungs, and, as a result, spinal anaesthesia or local anaesthesia was substituted for ether anaesthesia, or the operation was postponed.

Gosset, A., Ledoux-Lebard, R., and Bernard, E. (1938) *Bull. Acad. Méd. Paris*, **120**, 167

Pulmonary Embolism

T. H. Belt has published a further account of the routine examination at necropsies of the branches of the pulmonary arteries in the lungs; the opening of the secondary and tertiary branches had shown the high incidence of pulmonary embolism. Analysis of about 3,000 necropsies showed that at least 1 in 10 evidenced major or minor forms of embolism: a major embolism was one in which half or more of the pulmonary circulation was obstructed; a minor embolism was one in which less than half the pulmonary circulation was cut off. Two-thirds of the embolisms were major; but often a major embolism resulted from a shower of minor emboli. There was a general tendency to under-estimate the incidence and significance of the minor embolisms which were responsible for most of the haemorrhagic infarcts of

the lungs. Pulmonary embolisms were more frequent in medical than in surgical cases. The method of opening up the branches was described by Belt in 1936 when he had examined 1094 necropsies. Three groups were now described: (i) the majority of cases in bedridden patients of more than middle age with congestive heart failure; (ii) in cachectic patients; and (iii) post-operative embolism, causing sudden death. Probably 3 factors were at work in the complex mechanism of thrombosis, namely damage to the vessel walls, increased coagulability of the blood, and diminished velocity of the blood flow. Examination of many thrombosed veins failed to show evidence of any primary lesions in the walls of the affected veins.

Belt, T. H. (1936) *J. tech. Meth.*, **15**, 39.

— (1939) *Lancet*, **1**, 1259.

LUNG DISEASES: ACUTE INTERSTITIAL PNEUMONITIS

Clinical Picture

D. F. Smiley *et al.* reported the occurrence of 86 cases of acute interstitial pneumonitis occurring as an epidemic in a student body. The pulmonary lesions furnished no stethoscopic signs, but the process could be seen on an X-ray plate in the form of fan-shaped areas of increased density. As seen radiologically the infection spread outwards from the hilum, definite evidence not appearing until 36 or 48 hours after the clinical onset. The changes did not involve the periphery of the lung, and resolution occurred in 1 to 2 weeks. The disease began with malaise, weakness, and fever which, after one or 2 days, rose to 100 to 102° F. The patient then started to cough and complain of tightness in the chest. There was usually no sputum. In a second type of the disease the temperature was much higher and in a third type toxæmia was present with moist râles in the chest. A leucocytosis occurred, and the disease terminated by lysis. During convalescence many of the patients were very weak. It was suggested that the disease was identical with acute influenzal pneumonitis, acute pneumonitis, and the atypical pneumonia, probably caused by a filtrable virus, described by H. A. Reimann as occurring in Philadelphia in 1938.

J. Maxwell summarized the characteristics of 24 cases of pneumonitis, the condition occurring at any age, and cough being the predominant symptom. Sputum was usually slight and hæmoptysis uncommon. The lower lobes of the lung were more commonly affected, and areas of consolidation were found in 23 of the cases. Radiographically areas of local consolidation were seen, but in some cases the lesions were more diffuse and suggested tuberculosis. Pneumococci and mixed infections were found in the sputum. Complications were rare, but pleurisy, empyema, true pneumonia, and heart failure occurred in this series. The average duration of the disease was 2 weeks, and there were 2 deaths, one from true pneumonia and one from heart failure. The prognosis is much better than in true pneumonia.

Maxwell, J. (1938) *Lancet*, **2**, 239.

Reimann, H. A. (1938) *J. Amer. med. Ass.*, **111**, 2377.

Smiley, D. F., Showacre, E. C., Lee, W. F., and Ferris, H. W. (1939) *J. Amer. med. Ass.*, **112**, 1901.

LUNG DISEASES: CONGENITAL CYSTIC DISEASE

Ætiology

T. Holmes Sellors, in a comprehensive treatise on congenital cystic diseases of the lung, which he thinks might be more accurately described as 'congenital cystic diseases of the bronchi', states that the recognition of cystic diseases has only been noticeable during the last 10 or 15 years, owing to the increasing use of radiography. The fact that many examples are diagnosed early in life, apart from the rare cases which have been found in foetal existence, accounts largely for the term 'congenital'. More than 400 cases of this type have been recorded, so that the condition cannot be regarded as a medical curiosity.

He considers that the ætiological factor in the production of cystic disease of the lung lies in some developmental error of the bronchi. The ducts of Cuvier, lying in the lateral wall of the pleuro-pericardial sac, convey blood from the cardinal veins to the sinus venosus. An abnormality of the duct might cause pressure in

the developing main bronchus and the resulting partial broncho-stenosis may produce effects in the primitive lung distal to the block. If pressure occurs when the lobes are just appearing, a large cyst may be produced; the size of other cysts at birth would depend on the period of lung development at which the obstruction occurs. It is suggested that the developing lung might be subjected to pressure from the heart chambers and that cystic disease of the lung has been associated with congenital disease of the heart on several occasions. The author considers that cystic disease of the lung may be an atavistic condition or a reversion to a more primitive type of lung.

Morbid Anatomy

Sellers classified cases under the following headings (i) Solitary cysts, which are generally large: (a) huge 'balloon' or 'distension' cysts present in infants, and causing gross pressure signs and often death, (b) smaller cysts about the size of an orange, these may furnish no evidence unless infected. (ii) Multiple cysts, varying in size: (a) medium, in groups of 2 or 3, varying in size from a cherry to a golf-ball, and usually symptomless, (b) small cysts from the size of a currant to that of a cherry. These may follow a set distribution, which is usually lobar in character, in which case the cysts tend to be uniform in size and resemble a saccular bronchiectasis, or they may be diffuse or scattered, in which case the size of the cyst is variable (see Fig 17)

Complications

A survey of the various complications is given, and among the possible differential diagnoses the author mentions spontaneous pneumothorax, emphysematous bullae, tuberculous cavities, cavities created by pulmonary abscesses, diaphragmatic hernia, hydatid cysts, haematomas, carcinoma, and endothelioma. In discussing the histology of the condition, emphasis is laid on the uniformity of the lining membrane which maintains the character of bronchial epithelium. The bronchial wall shows considerable variation in the percentage, situation, and proportion of cartilage, muscle, and glands.

Treatment

The necessity for surgical treatment in all suitable cases is stressed, and also the value of bronchoscopy in diagnosis. In bilateral lesions in which surgical intervention is contra-indicated, the patient must be content with palliative treatment which includes avoidance of factors which encourage secondary respiratory infection, such as expectorants, postural drainage, and bronchoscopy.

Sellers, T. H. (1938) *Tubercle, Lond.*, **20**, 49, 114



FIG. 17—Congenital cystic disease of the lung, an oblique bronchogram showing scattered cystic spaces filled with contrast oil (From *Tubercle*, 1938)

LUNG DISEASES: PULMONARY EMBOLISM

Diagnosis

Radiography

N. Westermarck examined by X-rays 26 cases of pulmonary embolism shortly before death occurred. He divided his cases into those with infarct and those

without infarct, these 2 types having a different appearance. In cases of embolus of the pulmonary artery without infarct there is an ischaemia of the tissues supplied by the branches of the artery on the peripheral side of the embolus. This appears in the radiogram as a local and well-defined wedge-shaped zone with diminished or absent vascularization. The point of this wedge is directed towards the hilum, and the base to the periphery of the lung. In the case of a large embolus a whole lobe or the entire lung may be anaemic. In these cases there is a vascular shadow in the central parts of the lung only. In cases with infarct, this appears as a wedge-like massive homogeneous shadow. The wedge points to the hilum and has its base directed to the periphery of the lung. As an infarct is mostly found in lungs with stasis of the pulmonary circulation, the whole appearance is more congested than in the first case. If the infarct undergoes organization, a reactive inflammatory zone surrounds it, giving a more diffuse appearance to the former wedge. As the main criterion of early diagnosis of embolus of the pulmonary artery is a change of the vascular picture, diagnosis is very difficult because normal lung pictures sometimes show changes of vascularization similar to those in embolus without any pathological background.

Westermarck, N (1938) *Acta radiol., Stockh.*, **19**, 357

LUPUS VULGARIS

See also Vol. VIII, p. 254, and Cumulative Supplement, Key No. 1005.

Treatment

Injection of Starch

In view of the fact that starch is a good chemotactic agent for leucocytes in tissue culture, R. L. Kile decided to inject this substance into the nodules of lupus vulgaris. The report of a case is given in which a lesion the size of a man's palm involved the cheek and lobe of the ear, it had resisted all treatment, although some improvement resulted from the use of old tuberculin. Injections of starch suspension were made into 3 or 4 areas every 1 or 2 weeks, the amount used varying from 0.1 c cm. to 0.3 c cm. There were some slight reactions. Decided improvement was obvious from the beginning of this treatment, the centre becoming a smooth scar and only a few nodules persisting.

Kile, R. L. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 471.

LYMPHATIC GLANDS DISEASES

See also Vol. VIII, p. 264, and Cumulative Supplement, Key Nos. 1006–1009.

Tuberculous Adenitis

Treatment

Gelatin-acriflavine and calcium chloride—In order to secure early regression of enlarged tuberculous cervical glands (20 to 35 mm. in diameter) R. A. Hunter treated a group of 21 patients, of ages varying between 3 and 17, by injections of a medium composed of gelatin-acriflavine and calcium chloride (GACC). The periphery of the gland was first injected, then the deeper areas. Hardening of the gland usually occurred within 3 to 5 days after injection. The optimal dosage appeared to be 0.3 c cm. per injection, at intervals of 1 to 3 days. There need be no loss of school time. Pus formation occurred in only 3 cases and in 2 of these the gland had been very soft at examination. A group of presumably healthy children with a small degree of adenitis, possibly tuberculous, was treated by a course of 2 to 5 injections over a period of 2 to 4 weeks; 6 weeks later in 17 cases the glands had completely disappeared and in 11 they were definitely smaller.

Hunter, R. A. (1939) *Tubercle, Lond.*, **20**, 161.

Tumours

Classification

The primary tumours of lymphatic glands have been classified by J. Ewing as follows: (i) Lymphadenoma, which is not employed as a synonym for Hodgkin's

disease, but includes Brill's disease or the multiple giant follicular change described by Brill, Baehr, and Rosenthal in 1924 as splenomegalia lymphatica hyperplastica. This is a systemic disease, usually widely generalized, with moderate anaemia, mild fever, favourably influenced by irradiation, but recurring with increasing severity and usually proving fatal in 5 to 10 years. Histologically the lymph follicles are prominent, with hyperplastic germ centres and excessive lymphocytes, mainly normal. The other example of this lymphadenoma group is gastro-intestinal pseudo-leukaemia, a very remarkable systemic disease with myriads of small lymphomas, sometimes involving the whole alimentary tract without ulceration. Clinically the course is steadily progressive with some fever, anaemia, diarrhoea, emaciation, and death within a few months or years. Histologically the lymphoid follicles are well formed, composed of normal or large lymphocytes, and without the diffuse growth of malignancy or the ordinary type of systemic pseudo-leukaemia.

(ii) Lymphocytoma. This group contains a number of different clinical and morphological conditions, innocent such as a single lymphoma, malignant, beginning in a single gland and rapidly spreading to other glands. Systemic pseudo-leukaemia, plasmacytoma, and lymphocytic leukaemia are placed in this group. Ewing laid stress on the importance of tuberculosis in the aetiology of these lymphocytomas.

(iii) Reticulum-cell lymphosarcoma. This group contains the great majority of the lymphosarcomas. A noteworthy clinical feature is the healthy, robust, over-nourished appearance of these patients, which so strongly contrasts with most other forms of lymphatic disease, especially Hodgkin's disease. Histologically there is a diffuse growth of the reticulum cells with varying degrees of anaplasia.

Brill, N. L., Baehr, G., and Rosenthal, N. (1924) *Trans. Ass. Amer. Phys.* **39**, 371.

Ewing, J. (1939) *Bull. N. Y. Acad. Med.*, 2nd ser., **15**, 92.

LYMPHATIC VESSELS, DISEASES AND INJURIES

See also Vol. VIII, p. 278.

Lymphatic Destruction

Treatment

Intra-arterial injection of glycerin—The treatment of elephantiasis by the intra-arterial injection of glycerin is discussed by G. Bowesman. Its use is based on the property of glycerin of attracting tissue fluid from the tissue spaces towards the region in which the glycerin is placed. Injections of 10 per cent sterile glycerin in water were made into the femoral artery at weekly intervals. Pain did not occur if the injection was given slowly, and the optimal dose was found to be 2 to 3 c.cm. If larger doses were given, some pain in the region of the foot or knee, probably due to arterial spasm, was experienced. When it was found impossible to give intra-arterial injections, the solution was given intravenously. During the observation period, the affected limb was measured at regular intervals, and the results seemed to indicate that, if the condition had persisted for 2 years or less, improvement continued until the limbs became equal in size, whereas among those patients in whom the disease was from 2 to 4 years' duration there was considerable relief of the dull aching pain, with some reduction in size of the limb. No complications have been noted, and in those cases which have been followed up, the reduction has been maintained.

Bowesman, G. (1938) *Brit. J. Surg.*, **26**, 86.

LYMPHOPATHIA VENEREUM

See also Vol. VIII, p. 287, and p. 155 of this volume.

Aetiology

That lymphopathia venereum may be transmitted from parent to child was shown by two cases reported by Dick in 1936. In the first case both parents were infected, and when the child was 2 weeks old it showed a strongly positive Frei intradermal reaction. The second case was that of a girl of 14 discovered to have a rectal stenosis.

Her mother had died from intestinal perforation, having had a rectal stricture for 13 years. It is possible in this case that infection may have occurred post-partum between mother and child. W. E. Coutts and O. Monetta review these two cases and report a case of their own.

Coutts, W. E., and Monetta, O. (1938) *J. trop. Med. (Hyg.)*, **41**, 279.

Diagnosis and Differential Diagnosis

M. Paulson considered that the occurrence of a positive Frei reaction in association with conditions such as rectal stricture did not indicate with certainty that the lesion was due to lymphopathia venereum. It only showed that the patient had at some time been infected with the virus. Paulson considered that a positive bowel antigen was a better and more specific method of establishing the diagnosis in intestinal tissue. A bowel-discharge antigen is made up of inactivated blood, mucus, pus, and intestinal contents grossly free from faeces. Bowel-tissue antigen is made up of bowel tissue free from faecal contamination, macerated and inactivated. The author reported 5 cases in which lymphopathia venereum of the bowel was diagnosed by its use. The Frei reaction alone is not sufficient, because the patient who gives a negative reaction with it may give a positive reaction to bowel antigen.

Paulson, M. (1939) *J. Amer. med. Ass.*, **112**, 1788.

Treatment

Sulphanilamide

A. A. Knight and V. C. David reported 2 cases of lymphopathia venereum which were successfully treated with sulphanilamide. One patient suffered from rectal stricture and loose muco-purulent stools. The condition responded to a total dosage of 290 gr. of sulphanilamide, given during 7 days. The course was repeated in 10 to 14 days. After treatment there was no indication of abnormality of the rectal mucosa, and the stricture had disappeared. The second patient had sinuses and abscesses in the buttocks and genital area, and was cured by sulphanilamide. Both these cases had failed to respond to the routine treatment for lymphopathia venereum. The authors have also had other cases which responded dramatically to sulphanilamide therapy.

M & B 693

K. V. Earle treated successfully with M. & B. 693 2 West Indian males, aged 22 and 23 years, affected with lymphopathia venereum in an early stage, before fistulae had formed or any late complications had supervened. It was pointed out that the early stage of the disease was clearly the best period for successful treatment.

Anthiomaline

B. Shaffer *et al.* consider that anthiomaline, a trivalent compound of antimony, has several distinct advantages over other antimony preparations. It is given intramuscularly, its injection is painless, vomiting and laryngeal spasm do not occur, and its only reaction is 'antimony rheumatism', the severity of which determines the maximal dosage for the particular patient, and serves as an index of the patient's tolerance. Symptoms of a mild-grade secondary anaemia, at times accompanied by a slight eosinophilia, are sometimes found at the end of a long course of treatment. Anthiomaline is administered 2, or preferably 3, times a week. The initial dose is 0.06 g., and the amount is increased by 0.03 g. until the typical rheumatoid pains appear. This is a signal for the reduction of dosage until the pains are barely perceptible some hours after the injection. The average dose is 0.12 to 0.24 g. A course of injections totals 2 to 4 g., followed by an interval of 2 to 3 weeks, and perhaps by a further course of treatment.

It is shown that 50 to 60 per cent of cases show rapid cure under this treatment, with complete resolution of the inflammatory process within a period of 3 to 11 weeks as against the usual course of the disease which lasts 3 to 18 months. In addition to the inguinal syndrome the authors discuss anthiomaline therapy in cases of ano-rectal syndrome. Symptoms either rapidly disappeared or were greatly improved.

Earle, K. V. (1939) *Lancet*, **1**, 985.

Knight, A. A., and David, V. C. (1939) *J. Amer. med. Ass.*, **112**, 527.

Shaffer, B., Fonde, G. H., and Goldberg, L. C. (1938) *J. Urol.*, **40**, 863.

MALARIA

See also Vol. VIII, p. 304, Cumulative Supplement, Key Nos. 1018 and 1019; and p. 142 of this volume.

Diagnosis*From Respiratory Affections*

J. Frickler described 4 cases of malaria in which the symptoms closely simulated bronchitis and influenza, the signs being a dry cough, râles and rhonchi, and pyrexia. The apparent well-being of the patients, and the absence of the usual premonitory symptoms were marked. Treatment by quinine led to uneventful recovery.

Frickler, J. (1939) *Pr. méd.*, **47**, 967

Treatment*Prophylaxis*

Proseptasine—J. A. Sinton *et al* investigated the prophylactic action of proseptasine, a benzyl derivative of sulphanilamide, in experimental mosquito-borne malaria (*Plasmodium falciparum*). Three non-immune volunteers were given orally a total amount of 7.5 g. of proseptasine during the 24 hours before exposure to infected mosquitoes, and 4.5 g. of the drug during 2 hours after the mosquito bites; none of these subjects contracted malaria. Two other volunteers received 12 g. of the drug during the 24 hours before exposure and 15 g. during the subsequent 32 hours, and one of them developed malaria 22 days after infection. Lastly, 3 volunteers were given 9 g. in the 24 hours before exposure to mosquitoes, but did not have any more of the drug; 2 of them developed severe malaria 15 and 16 days later. The 5 subjects who escaped infection were under observation for 52 to 71 days. The controls, who did not have the prophylactic treatment, all contracted malaria. In 2 volunteers, proseptasine caused toxic symptoms—nausea, vomiting, headache—and, in one, an erythematous rash. These symptoms, however, disappeared 24 hours later. These observations showed that the drug had some degree of prophylactic action.

Cuative

Atebrin—A. T. W. Simeons gives his observations on the results of 'blanket' treatment of malaria with injectable atebirin over a period of two and a half years. The two original injections were followed by 0.01 g. of plasmoquine simplex on 3 consecutive days. Despite the highly malarious nature of the district, relapses were surprisingly low. As opposed to this, in cases of fresh malaria treated similarly in Bombay, although the immediate clinical results were highly satisfactory, there was a relapse rate of practically 100 per cent within 1 to 6 weeks. Oral treatment only, however, reduced the relapse rate to very low proportions. It is concluded that, in highly endemic or epidemic areas, the abbreviated 2-injection treatment yields excellent results, whereas in sporadic or first infections it is unsuccessful, and oral treatment is here recommended. The author feels that this points to an immunological factor.

Atebrin versus quinine.—O. T. Brosius has used quinine and atebirin in two series of cases of malaria, each 100 in number. Each series contained aestivo-autumnal, tertian, and quartan infections, and no distinction was made in choosing the group in which a case should be placed. One tablet of plasmoquine was given in all cases every night, and no incompatibility was shown between plasmoquine and atebirin or quinine. It was found that, taking the average, cases treated with atebirin showed permanently negative blood films earlier than those treated with quinine. It was further shown that no signs of toxicity appeared when using atebirin, most patients agreeing that it was more pleasant to take than quinine, and that gastric symptoms were slight, though more phlegmatic patients objected to this form of discomfort more than to the tinnitus aurium attendant on quinine administration. Relapses and reinfections were shown to be equal in the two series; both drugs appear to bring about substantial improvements in renal conditions. An important observation was that atebirin appeared to have no untoward effect upon the pregnant uterus as illustrated by the treatment of a young primipara who was almost at the end of the pregnant period. In cases of severe pernicious malaria the intramuscular or intravenous injection of quinine gives highly effective results. The economic factor is considered in all its aspects, and it is shown that the cost of atebirin therapy is lower

than that of quinine therapy, and that atebrian cases only remain in hospital two-thirds as long as quinine cases

Cinchona febrifuge.—R. N. Gore recorded his experience with the use of cinchona febrifuge powder in malaria. The dosage employed in an adult was a 4 gr. tablet, 3 times a day for a week, then one twice a day for a fortnight, and finally one tablet a day for a further week. Good results were obtained. Not only was a rapid reduction of fever obtained, but the spleen was reduced in size by half, and relapses were prevented. The febrifuge has a markedly laxative effect. The best results with cinchona febrifuge were obtained if a preliminary dose of 3 gr. of quinine hydrochloride was given at the commencement of the rigor or fever. The powder can be made into a paste or pill with honey.

Prontosil. W. F. B. Hall reported 4 patients with general paralysis of the insane who were given prontosil during malaria treatment after the rigors were well marked. The object of the investigation was to test the action of the sulphonamide group in tertian malaria, and he concluded that the drug had not any place in its treatment. The patients were given prontosil by mouth and prontosil intramuscularly in 2 cases, prontosil alone in one case, and prontosil only in the other. All the attacks had to be terminated with quinine, and the sulphonamides did not reduce the number of parasites in the blood. Hall quoted the results of other observers, the majority of which confirmed his experience.

Hall's results are confirmed by those of J. C. Niven who compared the results of the treatment of 80 cases of acute malaria with prontosil, and 68 with quinine dihydrochloride. The investigation showed that prontosil has some lethal action on malaria parasites, being more marked against *P. falciparum* than against *P. vivax*. But mosquitoes fed on "crescent" carriers who had been given prontosil for 7 days were easily infected. No toxic effects were seen in patients treated by prontosil but Niven concluded that, owing to this possibility and its low efficiency and high cost by contrast with quinine, prontosil has no place in the treatment of malaria.

Brosius, O. T. (1938) *Ann intern Med.*, **12**, 353.

Gore, R. N. (1938) *Indian med Gaz.*, **73**, 608.

Hall, W. F. B. (1938) *J. Pharmacol.*, **63**, 353.

Niven, J. C. (1938) *Trans R. Soc. Trop. Med. Hyg.*, **32**, 413.

Simeons, A. T. W. (1938) *Indian med Gaz.*, **73**, 713.

Sinton, J. A., Hutton, F. L., and Shute, P. G. (1939) *Ann trop Med Parasit.*, **33**, 37.

Malaria Therapy

Control by Thio-bismol

During treatment of patients with syphilis of the central nervous system by malarial therapy, it was found that thio-bismol exerted an antimalarial influence, and eliminated, or markedly decreased the intensity of, paroxysms. In 7 out of 15 patients with daily cycles, it was demonstrated that alternate paroxysms were affected. The patient's general condition was improved and the subsequent course of treatment was well tolerated. It is suggested that injections of thio-bismol might be of use in cases of therapeutic malaria in which severe reactions were experienced or the patient suffered exhaustion. In the series investigated by W. F. Schwartz there were 21 patients with therapeutic malaria of the tertian variety, and 2 with epidemic malaria. In all these, the first injection of thio-bismol produced an alteration in the succeeding malarial cycle, and in none did the usual sustained prodromal temperature-rise occur. The remaining cycle was altered in some cases by a further single injection, but, when this failed, repeated injections inhibited the paroxysms as long as the injections were continued. The antimalarial action of thio-bismol could not be attributed to either the bismuth or to the thioglycollate. When given separately, neither component affected the course of the disease.

Schwartz, W. F. (1939) *J. Pharmacol.*, **65**, 175.

MEASLES

See also Vol. VIII, p. 412, Cumulative Supplement, Key No. 1027, and p. 77 of this volume.

Complications

F. W. Goodpasture *et al.* recorded 5 cases of a previously undescribed form of

respiratory disease in patients under the age of 2½ years, due to a virus infection superimposed on an epidemic infection, particularly measles and whooping-cough. The lesions in the respiratory tract showed that, notwithstanding the bacterial infection, a specific virus determined the fairly distinctive changes present both grossly and microscopically. Hyperaemia of the tracheal mucosa, epithelial necrosis, ulceration of the tracheal and bronchial mucosa, subsequently interstitial pneumonia, and characteristic intranuclear inclusions present almost exclusively in the epithelial cells of the trachea and bronchi and pulmonary alveoli were essential details. The virus in the 5 cases differed from that of simple herpes and the so-called inclusion disease of infants. It was thought to be becoming more frequent.

Goodpasture, F. W., Auerbach, S. H., Swanson, H. S., and Cotter, E. F. (1939) *Amer. J. Dis. Child.*, **57**, 997.

Treatment

Prophylaxis

Convalescent serum.—J. L. Kohn *et al.*, impressed by the results obtained from the intravenous injection of adequate amounts of convalescent measles serum given in the pre-eruptive stage of measles, carried this out in 24 children, with definite modification in 19. The effective dose was 40 to 50 c cm given at least one day before the appearance of the eruption. In most cases fever persisted only 2 days after the injection, as compared with an expected duration of 4 days. There were no subsequent cases of pulmonary involvement. The injection of convalescent serum on successive days appeared to have an additional effect, but normal adult serum given in equal volume to that of measles convalescent serum did not cause any modification. Administration of 150 to 210 c cm of normal serum concentrated to one-third of its volume was effective in only 1, or possibly 2, out of 4 patients. There is no risk from the intravenous injection of large quantities of properly-prepared pooled human serum. This procedure is specially valuable in weak or debilitated children, in those who have just recovered from whooping-cough and other infectious diseases of childhood, and in those in whom measles has developed during the course of another acute or chronic disease.

Placental extract. T. N. Parish described the prophylactic effect of placental extract in an epidemic of measles in a girls' school. One intramuscular injection of 4 c cm of Lederle's immune globulin was given intragluteally. The extract was found to have no effect in preventing measles. Of the susceptible children who were inoculated, 93 per cent developed measles, but, of the susceptible children not inoculated, only 75 per cent developed the disease. Cases occurring within 3 or 4 weeks of injection appeared extremely mild. Conjunctivitis and persistent bronchitis were rarer in the inoculated cases, and the pyrexia seemed to vanish more quickly.

Kohn, J. L., Klein, I. F., and Schwarz, H. (1938) *J. Amer. med. Ass.*, **111**, 2361.

Parish, T. N. (1938) *Brit. med. J.*, **2**, 65.

MEDIASTINUM DISEASES

See also Vol. VIII, p. 438.

Tumours

Clinical Picture

Compression of brachial plexus. J. M. Miller *et al.* record the case of a woman, 25 years old, with compression of the brachial plexus by an isolated metastasis from a primary adeno-carcinoma of the lung. The clinical picture was that known as 'superior sulcus tumour', or a tumour appearing in the region of the upper opening of the thorax, usually originating from a terminal bronchiole in the apex of the lung. The clinical features were pain in the shoulder or chest on the affected side, weakness or atrophy of the muscles of the upper extremity, and Horner's syndrome, due to involvement of the cervical sympathetic and consisting of miosis of the pupil, enophthalmos, and ptosis palpebrae. These symptoms might be due to several other causes, such as a cervical rib, trauma, the scalenus anticus syndrome, and primary neoplasms of the spinal cord and meninges, or of the cervical or thoracic vertebrae. Symptoms of a primary tumour of the lung, such as cough and

haemoptysis, might be absent, but this should not exclude diagnosis of a primary tumour of the lung.

Miller, J. M., Frugoni, P., and Craig, W. McK (1939) *Proc. Mayo Clin.*, **14**, 161.

MEDICO-LEGAL EXAMINATIONS AND REPORTS

See also Vol VIII, p 453, and Cumulative Supplement, Key No 1030.

Detection of Spermatozoa in Seminal Stains

Experiments were carried out by S. N. Chakravarti and S. N. Roy for the detection of spermatozoa in seminal stains kept in the dry and wet states, and in seminal stains containing blood kept in the dry state and similar stains kept in a wet state. Four pieces of cloth were used. Complete spermatozoa were detected on the two dry cloths after 100 days, but the mixed blood and semen stains were negative to the Florence test after 44 days. In the wet state both seminal stains alone and blood and semen mixed gave a negative Florence test after 48 hours, while the tails began to disappear after 10 days and were unrecognizable after 75 days, although clear heads could be detected after 100 days. The importance of drying material before sending it for examination was stressed, and also the lack of conclusive evidence given by the Florence test in wet or old stains.

Chakravarti, S. N., and Roy, S. N. (1938) *Indian med. Gaz.*, **73**, 412.

MEGACOLON AND ANAL ACHALASIA

See also Vol VIII, p. 470, and Cumulative Supplement, Key No. 1031.

Treatment

Parasympathetic Paralysants

W. O. Klingman reviews the literature on the subject of megacolon from Hirschsprung (1888) up to the present day. Whether the condition is congenital or acquired, strong support is given to the hypothesis postulating its neurogenic origin. The results of lumbar sympathectomy and ganglionectomy supported this contention. The aetiology remains obscure, but it is suggested that the dilatation and hypertrophy of the colon are compensatory changes which arise in an attempt to remove the faecal content. Further advances both in the study of the autonomic nervous system and in pharmacology have suggested new methods of attack on the problem of megacolon with constipation, by the use of drugs of cholinergic and anticholinergic type. All the cases studied by the author showed the same symptoms—severe constipation (bowel movement usually obtained only by enema), abdominal distension, visible peristalsis, muscle atrophy of the abdominal wall, toxic symptoms, spastic or hypertonic anal sphincter, and X-ray findings of megacolon after barium enema. In cases in which neurogenic imbalance exists because of faulty inhibitory or motor function of the parasympathetic system, selective drug therapy has proved effective. Treatment consisted of giving parasympathetic paralysants. Atropine is cited as the drug of choice in inhibiting acetylcholine but its highly toxic effect contra-indicates administration, and syntropan (the 3-diethylamino-2, 2-dimethylpropanol ester of tropic acid), given by mouth was substituted. When the symptoms pointed to a weakness in the expulsive musculature of the colon above the recto-sigmoidal region, prostigmin was the drug selected. A record is given of satisfactory results in 7 cases.

Klingman, W. O. (1938) *J. Pediat.*, **13**, 805.

MENINGITIS

See also Vol. VIII, p 495, Cumulative Supplement, Key Nos. 1033–1040; and p. 125 of this volume.

Pneumococcal Meningitis

Bacteriology

According to Joppich infantile pneumococcal meningitis is second in frequency among the forms of meningitis in infancy, and is almost always fatal. As recovery

may follow meningococcal meningitis, it is concluded that the type of infecting organism is more important than the localization of the disease. As specific serum treatment would be of the utmost importance, he investigated the types of pneumococci in 28 fatal cases of infantile pneumococcal meningitis, and found that the following types of pneumococcus may be responsible: I, III, IV, V, VI, VII, VIII, X, XIV, XVIII, XIX, XX, and XXVIII. It would therefore be practically impossible to prepare a serum specific for every one of these types. As the available multivalent sera are mainly directed against type I and in a lesser degree against type II, specific serum treatment in infantile pneumococcal infections is unlikely to prove of any practical value.

Treatment

Sulphonamide drugs—D. McAlpine and G. C. Thomas reported pneumococcal meningitis in a man of 24 treated with M & B 693. This treatment began on the third day of the illness and 36 hours later the temperature became normal. The signs of meningitis had finally cleared by the fifth day of treatment after 19 g. of the drug had been given. The amount of M & B 693 employed was 25.5 g. spread over 7 days and the maximal concentration of the drug in the cerebrospinal fluid was 3 mg. per 100 c.cm. The daily dose was 5 to 6 g. for the first 2 days, continued with decreasing doses for 3 to 4 days after the temperature was normal. This drug had fundamentally altered what had previously been considered to be an almost invariably fatal prognosis. Emphasis was laid on the urgency of early diagnosis of the disease and the empirical use of M & B 693 in all cases. Lumbar puncture should be performed at the commencement of treatment to confirm the diagnosis but subsequently it should only be used at intervals of 3 days to determine the effect of the drug on the pneumococcus and the cell count.

H. Dunlop and J. Laurie also treated a case of pneumococcal meningitis with M & B 693. The right frontal sinus, which was full of pus, was drained, and the drug was given daily from the time of admission. On the day after operation, the temperature fell to normal, and 4 days after admission the cerebrospinal fluid contained no organisms, whereas on admission it had contained pneumococci and *B. veiosis*. Four days later the drug was discontinued, a total of 24.5 g. having been given. Thirty-six hours afterwards the temperature rose again, organisms appearing in the cerebrospinal fluid. The drug was continued for 9 days, making the total dosage 40.5 g. The condition improved, and the patient was discharged in good health after 7 weeks in hospital. Anaemia developed a week after admission, and was successfully treated by a blood transfusion.

P. S. Raman adds a further case to the list of successes claimed for M & B 693 in pneumococcal meningitis. The patient was a Hindu coolie, aged 34, admitted to hospital on January 30. The 15 previous admissions of this type had all terminated fatally. Lumbar puncture was carried out daily. Two g. of M & B 693 were given following admission, and then 1 g. every 3 hours. The tablets, crushed in milk, were administered through a nasal tube until the patient was capable of taking them orally. The patient was sitting up in bed taking feeds by February 1, temperature was normal on the 2nd, and the cerebrospinal fluid was sterile from February 13. The quantity of the drug was reduced to 1 g., 3 times a day, on the 8th, and the drug itself was finally discontinued on the 13th. As a relapse occurred the following day, it was necessary to resume treatment for another 14 days before complete ultimate therapeutic success was attained. The total quantity of M & B 693 used in the first attack was 80 g., and in the relapse a further 75 g.

Surgery and vaccines—J. Gubner reported a case of Type III pneumococcal meningitis following mastoiditis from which the patient recovered although the mortality for this condition is usually 100 per cent. He recommended prophylaxis in these cases by wide and early surgical eradication of the infective focus in the mastoid antrum when early meningitis was suspected, and injection of an autogenous vaccine. In established meningitis a lumbar puncture should be carried out daily. Drainage of the cerebrospinal fluid by more drastic measures, such as cisternal puncture, was condemned. Small blood transfusions favoured a return to normal of the cerebrospinal fluid, and maintained the haemoglobin level which might be reduced by production of methaemoglobin as a result of sulphanilamide treatment. Sulphanilamide was recommended in this type of meningitis, sufficient being given to keep the blood content at 8 to 10 mg. per 100 c.cm.

Dunlop, H., and Laurie, J. (1939) *Lancet*, **1**, 1437.

Gubner, J. (1938) *Arch. Otolaryng.*, Chicago, **28**, 241.

Joppich (1938) *Klin. Wschr.*, **17**, 1757.

McAlpine, D., and Thomas, G. C. (1939) *Lancet*, **1**, 754.

Raman, P. S. (1939) *Lancet*, **1**, 1101.

Pyogenic Meningitis

Aetiology

In an article with a wealth of historical and statistical data R. W. Teed has collected 129 cases of suppurative meningitis and 2 of serous meningitis which, if the patient had lived longer, undoubtedly would have become purulent, the previous number of collected cases was 47 (Hajek). Meningitis was by far the commonest intracranial complication of disease of the sphenoidal sinus. There were among the cases of meningitis 7 instances of extradural abscess, 7 of cerebral and 1 of cerebellar abscess, and 6 of suppurative and 1 of haemorrhagic encephalitis. There were 20 cases with concomitant otitis and 47 with purulent thrombosis of the cavernous sinus. In 2 cases the internal carotid artery in the diseased cavernous sinus was also thrombosed. Glycosuria, which might be due to involvement of the pituitary or of the hypothalamus, was previously reported in 3 cases, and details of 3 new cases were added. Only one case of meningitis due to sphenoidal sinus disease had undergone spontaneous cure, but 7 patients recovered after the sphenoidal sinus had been treated surgically. Inflammation of the sphenoidal sinus was not very common; statistics showed that it occurred in 15.7 per cent of cases recognized clinically, and in 22 per cent of cases in which it was found at necropsy.

Treatment

Sulphonamide drugs.—R. Debré and J. Marie state that the mortality of streptococcal meningitis treated unspecifically is about 90 to 100 per cent and strongly advise treating this type of meningitis with a sulphonamide preparation, para-aminophenylsulphamide. The preparation is absorbed by the mucous membrane of the mouth. Large doses should be given for long periods. The dosage for adults is 8 to 12 g. in 24 hours for a period of 15 to 25 days, the dosage for children 0.15 g. per kilo body-weight (i.e. approximately 1 gr. per lb) for a period of 15 to 25 days. Injections of a 0.85 per cent solution (15 to 30 c.cm.) into the arachnoid membrane are also recommended. If the patient is unable to take the preparation by mouth, suppositories containing 1 g. of the drug, and sub-arachnoid injections should be given. As the substance is rather toxic, cyanosis will occur in most patients; this is not an indication for reducing the dose. If skin eruptions, thermic reactions, or icterus occur, the drug should be discontinued. No other medication is necessary, except occasionally cardiac tonics. The results are described as hopeful.

G. M. Retan made some investigations with the object of determining the proper dosage and best method of giving sulphanilamide in streptococcal meningitis, in which it is said to have reduced the mortality from 97 to 20 per cent. Intravenous injection of hypotonic sodium chloride solution reduces the osmotic pressure of the blood, causing a continuous flow of fluid from the capillaries into the pericellular tissue spaces of the central nervous system. In inflamed tissue the capillaries are particularly permeable; sulphanilamide added to the solution passes rapidly into the inflamed areas. By experiments on monkeys, Retan showed that, if sulphanilamide and physiological saline were injected intravenously, the concentration of sulphanilamide was greater in the blood than in the cerebrospinal fluid, when hypotonic saline solution was used, after the first injection the relative concentrations were the same as with physiological saline, but, when the injection was repeated on the next day, the concentration in the cerebrospinal fluid became higher than in the blood. When sulphanilamide was given by mouth and hypotonic saline intravenously the result was the same. The author described a case successfully treated by this means, and recommended that a 0.375 per cent solution of sodium chloride should be used. The rate of injection should be 10 c.cm. per pound body-weight per hour, but never more than 1 litre per hour. The treatment should be continued for 5-hourly periods with several hours' rest interval between each. Lumbar puncture should be performed during the treatment, and, if the pressure of the cerebrospinal fluid is considerably raised, 5 to 10 c.cm. should be withdrawn during a half-hour period.

Surgical.—P. Sacks emphasized the importance of early removal of the initial lesion in haemolytic streptococcal meningitis. Headache and vomiting during the course of aural infection should suggest intracranial involvement, probably meningitis. In

otic sepsis due to involvement of the sigmoid sinus, the primary focus being in the blood stream, the infected sinus should be incised. When the primary focus is in the cerebrospinal fluid, the nearest collection of that fluid should be evacuated by incision of the dura. The symptoms of suppuration of the petrous pyramid and the labyrinth should be recognized as both lend themselves to surgical drainage. In the elimination of a mastoid lesion Sacks considered it very important to remove all limiting bone plates from the zygoma anteriorly, to and beyond the sinus posteriorly. This procedure eliminated possible foci of osteo-thrombophlebitis which might lead to infection of the meninges. In the treatment of septic meningitis Eagleton and Shambaugh, Jr., incised the dura adjacent to the initial focus. If this was combined with sulphanilamide more recoveries resulted. Sacks reported a case in which sulphanilamide was used intraspinally and without causing any irritating effect in the meninges

- Debré, R., and Maric, J. (1938) *Schweiz. med. Wschr.*, **68**, 1342.
 Hajek, M. (1915) *Pathologie und Therapie der entzündlichen Erkrankungen der Nebenhöhlen der Nase*, p. 438.
 Retan, G. M. (1938) *Amer. J. Dis. Child.*, **56**, 483.
 Sacks, P. (1938) *Arch. Otolaryng.*, Chicago, **28**, 364.
 Teed, R. W. (1938) *Arch. Otolaryng.*, Chicago, **28**, 589

Meningococcal Meningitis

Treatment

Serum and sulphanilamide—H S. Banks treated 38 cases of acute meningococcal meningitis with serum given either intravenously or by the lumbar, cisternal, or, occasionally, ventricular routes; 59 other cases with intravenous serum and oral sulphanilamide, and 16 cases with sulphanilamide alone. In the first group the mortality-rate was 16 per cent. The cerebrospinal fluid was usually sterile within 24 to 48 hours. In about 20 per cent of this group meningococci persisted for several days. In the second group the mortality-rate was 11·8 per cent. The cerebrospinal fluid was sterile within 24 hours, except in a few cases which received small doses of sulphanilamide, and recovery was speedy in this group. In the third group 15 of the cases recovered rapidly. The most favourable age-period in all 3 series was from 5 to 20. Banks concluded that sulphanilamide was a very effective form of treatment for this disease in both Group I and Group II infections. The initial dosage should be high, the level of sulphanilamide concentration in the cerebrospinal fluid should be 5 mg. per 100 c.cm. within 24 hours and should be maintained for 3 days. Combined sulphanilamide and serum therapy was very effective, especially in severe cases in both Group I and Group II infections. When serum is used, it should be given in one or two large doses either intravenously or intraperitoneally. Lumbar punctures, repeated daily for 2 or 3 days, were carried out in some cases, but, apart from that, drainage was rarely necessary.

Banks, H. S. (1938) *Lancet*, **2**, 7

Non-Bacterial Meningitis

Types

G. Fanconi describes various cases of endemic poliomyelitis which is the most important type of non-bacterial meningitis. He gives a list of the types of non-bacterial meningitis as follows. (i) Meningitis with very few bacteria—demonstration of bacteria impossible: (a) meningococcal, (b) spirochaeta Weil type, (c) luetic meningitis; (d) meningitis serosa discreta tuberculosa, and (e) meningitis during convalescence from streptococcal meningitis. (ii) Meningitis concomitans or sympathica: (a) in otitis, sinusitis, osteomyelitis of the skull; (b) in brain tumour or abscess; and (c) in acute or subacute encephalitis (disseminated sclerosis). (iii) Toxic allergic meningitis: (a) after intralumbar serum injections; (b) in poisoning (lead, carbon monoxide); (c) in auto-intoxication (uraemia, diabetic coma), (d) in helminthiasis; (e) in acute infective diseases (pneumonia, influenza); and (f) meningitis serosa in tuberculosis. (iv) Meningitis caused by physical influences: (a) meningitis after lumbar puncture; (b) inflation of air into the spinal medulla; (c) bleeding; (d) trauma; and (e) sunstroke. (v) Virus meningitis: (a) epidemic poliomyelitis; (b) a virus meningitis, called 'swineherd's disease', caused by a virus similar to that of Rocky mountain spotted fever; (c) meningitis lymphocytaria; (d) syndrome of

Guillain-Barré (polyradiculo-neuritis); and (e) secondary meningitis in mumps, measles, herpes zoster, etc.

Fanconi, G. (1938) *Schweiz. med. Wschr.*, **68**, 929.

MENORRHAGIA AND METRORRHAGIA

See also Vol VIII, p 508.

Menorrhagia

Treatment

Oestrogen and progesterone.—It is believed that in many patients functional irregularities of uterine bleeding are due to gonadotrophic and endometriotrophic influences. Many sex-steroids have been used in the treatment of this type of bleeding, mainly without effect. E. C. Hamblen treated 12 such patients by the cyclical administration of oestrogen and progesterone, or with progesterone alone. The bleeding was stopped by curettage or oestrogenic therapy, and, one week after the cessation of all bleeding, 10,000 to 20,000 I.U. of oestrogenic substance was given daily for 14 days. Progesterone was then given daily in doses of 5 I.U. for 7 days. Bleeding usually occurred before the conclusion of this treatment, on which the progesterone was stopped, and no treatment was given during the week of the bleeding. One week after the onset of haemorrhage the treatment was begun again. If the bleeding had not stopped after 7 days, oestrogen was given to terminate it. Those patients receiving progesterone only received the same dose, and it was begun 3 weeks after the bleeding stopped. All 12 patients were benefited by the treatment. Seven of them, after periods of 2 to 10 months without treatment, still had no return of the meno-metrorrhagia. Endometrial biopsy before, during, and after treatment showed that this therapy rendered the endometrial cycle more nearly normal.

T. N. MacGregor treated with progesterone 5 cases of ovular bleeding, 7 cases of anovular bleeding, and one case of menorrhagia of puberty. Five mg. daily was the optimal dose, and this was given 2 or 3 days before the expected bleeding in the ovular cases, and at any stage in the anovular. In the latter group it was given until the bleeding was controlled and then a total dosage of 25 to 30 mg. was given during the amenorrhoeic phase. In the ovular group 3 patients had had a regular catamenia for the last 18 to 22 months, and the other 2 benefited from the treatment. In the anovular group 4 cases became regular and normal in menstruation, but in 2 of these there had been a recurrence of irregularity. In the other 3 cases in this group the endometrium became more normal; 2 of them had had two normal periods while under treatment, and the third had had one normal period. The case of menorrhagia of puberty did not respond to progesterone, but her periods had become regularized after treatment with oestradiol benzoate.

Autohaemotherapy.—I. P. Doneddu treated menorrhagia in 16 girls by autohaemotherapy. At first 10 c.cm., and later 20 c.cm., were taken from the arm vein and injected intramuscularly, measures being taken to combat anaemia. The menorrhagia stopped after a few days, menstruation occurred regularly, and the general condition improved. It was suggested that menorrhagia during puberty was due to changes in the endocrine and autonomic nervous system which were corrected by the injection of the patient's own blood (especially the plasma). Colloidal equilibrium was also brought about by the injection. The injection of the patient's own blood was regarded as a combined hormone and serum therapy.

X-irradiation.—According to T. F. Todd the dosage of X-rays necessary to ensure permanent amenorrhoea in a woman of 40 is about 500 r. X-rays may be administered to an out-patient in 2 or 3 short treatments, and may be applied accurately to the ovaries without affecting the uterus in any way. Permanent amenorrhoea results after 1 to 3 months. Radium therapy may be followed by haemorrhages from telangiectases and the endometrium, overdosage in one case caused an extensive radionecrosis. The treatment must not be undertaken in the presence of inflammation of the fallopian tubes.

Doneddu, I. P. (1937) *Ann. Ostet. Gynec.*, **59**, 787.

Hamblen, E. C. (1939) *Endocrinology*, **24**, 13.

MacGregor, T. N. (1938) *Brit. med. J.*, **2**, 116.

Todd, T. F. (1938) *Lancet*, **2**, 821.

Metrorrhagia

Treatment

Testosterone propionate.—The use of testosterone propionate in the treatment of functional uterine haemorrhage was investigated by S. H. Geist *et al.* Twenty-five cases were studied, 4 of which revealed small intramural myomas. Doses of 300 to 1,000 mg. per month were given. Excessive bleeding was controlled in all but 2 cases and normal menses were established in 18. In 5 cases amenorrhoea of 1 to 5 months' duration resulted, and 2 were unaffected by the treatment. Curettage was performed before testosterone propionate was given, and revealed a secretory phase pre-menstrually in 18, endometrial hyperplasia in 2, and a proliferative phase in 3 cases. Curettage after treatment showed that testosterone propionate inhibits menstruation and arrests the endometrium at the early proliferative phase. Large doses caused varying degrees of regression up to atrophy. If the treatment is stopped the inhibitory effect disappears. The authors suggested that testosterone propionate produced these changes by inhibiting the gonadotrophic factors of the pituitary, causing suppression of the ovarian cycle with consequent cessation of production of oestrogen and progesterone.

C. Mazer and M. Mazer treated 38 women suffering from metrorrhagia with 30 to 300 mg. per month of testosterone propionate in sesame oil, injected intramuscularly 3 times weekly, in doses of 2.5 to 25 mg. for 2 to 9 weeks. Sixty-eight per cent of the patients were cured, and the remaining 32 per cent were either relieved temporarily, or not affected by the treatment. Preliminary curettage apparently increased the likelihood of cure. The authors issue a warning against using too large a dose of the hormone, as symptoms of masculine change, such as growth of hair on the face, might occur. They found that smaller doses of 30 to 120 mg. were sufficient to relieve symptoms, and this dosage appeared to affect the uterus directly, and not through the anterior pituitary lobe.

Geist, S. H., Salmon, U. J., and Gaines, J. A. (1938) *Endocrinology*, **23**, 784.

Mazer, C., and Mazer, M. (1939) *Endocrinology*, **24**, 599.

MENTAL DEFICIENCY

See also Vol. VIII, p. 520, and Cumulative Supplement, Key Nos. 1044-1056

General Clinical Picture

Associated Skin Diseases

T. Butterworth and McC. Wilson, Jr., examined the skin and accessible mucous membranes of 1,895 feeble-minded persons, 44 per cent females and 56 per cent males, the majority being between 20 and 30 years of age. In 654 individuals, 780 dermatological conditions were diagnosed, and 68 different conditions were found. Acne vulgaris was the commonest of these, the sex incidence being equal. Many types of vascular and non-vascular naevi comprised 140 of the cases. Tinea or ringworm was the next most frequent lesion encountered, 63 cases occurred, and, of these, 34 were tinea versicolor. The disease had an epidemiological distribution, and prompt isolation of 5 cases of ringworm of the scalp prevented its spread. The incidence of ringworm of the feet was very low, only 14 cases. Pyodermitis, including all pyogenic skin infections such as impetigo and furuncle, occurred in 53 patients. The feeble-minded appear to have a lowered resistance to pyogenic organisms, and small abrasions often become infected. They also spread these lesions by picking at them. Striae distensae were seen in 39 patients, nearly all adolescent girls. Thirty of the patients had gained weight since admission, and 9 had lost weight. It was not known whether the atrophic striae appeared before or after the loss of weight in the last group. Dermatitis traumatica was noted in 30 patients, caused by the patients injuring themselves when annoyed or tormented. They bite their hands and wrists, and the skin in this region becomes erythematous, thickened, dry, and hyperkeratotic. The thickening often takes on the pattern of the patient's teeth. In some cases atrophic scars form, and, in these cases, the trauma has been greater, and lacerations have been produced. Common warts occurred in 17 patients, and flat juvenile warts in 3. No plantar warts were noted. Hypertrichosis occurred in 12 males and 5 females. Low hair lines, fusion of the eyebrows, and abnormal distribution of the pubic hair were also seen. Perlèche was the ninth most common skin

disease. The feeble-minded often dribble, and the skin at the corners of the mouth becomes softened, and secondary fissures develop. Most of the cases occurred in young children. Sixteen cases of molluscum contagiosum were found, but, at the time of the survey, an outbreak was in progress. Butterworth and Wilson believed that in the normal course of events seborrhoea would have occupied the tenth place in the list of the 10 commonest skin diseases among the feeble-minded. Among rarer conditions encountered were urticaria, herpes, neurofibromatosis, and vasomotor changes resulting in clamminess and blueness of the hands and feet.

Butterworth, T., and Wilson, McC., Jnr (1938) *Arch Derm Syph*,
N Y, **38**, 203

Mongolism

Aetiology

C. E. Benda (1938) studied 120 mongols from clinical measurements, radiographs of the bones, and necropsies. The results were classified according to the age of the patient. He found that the influence which leads to the condition of mongolism is predominant during ante-natal life. Many of these children die in the first year. Growth previously normal, if slow, was retarded after about the age of 9 in these children, but their weight from the fifth year was excessive, dystrophia adiposo-genitalis often developing after puberty. Benda found that the mongoloid skull is not microcephalic at birth, but that it shows retardation of growth due to arrest in development of the base of the skull, and, after 6 months, all mongoloid children appear microcephalic. The fibrous parts of the skull also took part in the general disturbance of growth, and he found that the peculiar appearance of the skull was due to the abnormal position and contour of the base of the skull and of the orbits. He concluded that the shape of the skull was due to disturbance during foetal development, and was unconnected with the mongol race or any kind of atavistic regression. X-ray examination of the carpal bones showed irregular ossification in this series. Mongoloids usually show early ossification.

A. A. Werner *et al.* treated 8 mongol children with anterior pituitary extract and thyroid extract, and observed them for 4 years. During that period they grew in height and weight approximately to the same extent as normal children of the same age. The mental age and intelligence quotient were unaltered by the treatment. Five mongol children receiving no pituitary extract or thyroid were observed for 4 years; their average increase in height and weight was not significantly less than that of the treated children or of normal children. The results suggest that in mongol children there is a sufficient amount of the growth factor in the pituitary.

Morbid Anatomy

Thyroid and pituitary.—C. E. Benda (1939) found that the thyroid in mongols showed (i) in the first 2 years of life irregular parenchymatous growth without the formation of vesicles, a number of greatly enlarged tubules, and fibrosis, and (ii) in mongols over the age of 6 years the vesicles are distended with colloid which is also present in the interstitial tissue, the thyroid as a whole being small and underdeveloped. In 13 cases the pituitary was not enlarged, but microscopically the basophils were deficient in number with probably a resulting apparent increase of the eosinophil cells.

Benda, C. E. (1939) *Arch Neurol. Psychiat.*, Chicago, **41**, 83

— (1939) *ibid.*, **42**, 1.

Werner, A. A., Lewald, J., Johns, G. A., and Kelling, D. (1939) *Amer. J. Dis. Child*, **57**, 554.

METABOLISM, BASAL

See also Vol VIII, p. 588

Relation to Fall in Blood Cholesterol

In an attempt to appraise the relation between the rise in basal metabolism and the fall in blood cholesterol which is exhibited in cases of hyperthyroidism, K. S. Harrison conducted a series of experiments on 5 patients, in each of whom thyroid deficiency was apparent. One thousand units of thyrotrophic hormone were administered each day for 4 days. It was found that the patients, whose low basal metabolic

rate was due to primary pituitary deficiency, responded to this therapy, and a definite rise in the rate of metabolism ensued. In 2 patients, in whom the low metabolic rate was due to spontaneous hypothyroidism, no rise occurred in the first, and only a slight rise in the second. In a patient whose thyroid gland had been removed no rise occurred. It was concluded that thyrotrophic hormone is only of value if the gland is present and capable of stimulation. Four of these patients showed a definite fall in blood cholesterol, the fifth showed only a very slight decrease. The last had undergone thyroidectomy one year earlier. Administration of thyroxine caused an immediate rise in the basal metabolic rate in this case. The degree of rise in the metabolic rate did not necessarily correspond with the fall in blood cholesterol. This was especially noted in one case of hypothyroidism in which no rise in that rate occurred, yet the blood cholesterol fell from 340 to 237 mg. per 100 c cm. The author suggested that the cholesterol level of the blood might have responded to slight thyroid activity, whereas the metabolic rate needed more pronounced stimulation. Alternatively the thyrotrophic hormone might have acted directly on the blood cholesterol level, or indirectly through the adrenal or other endocrine glands.

Harrison, K. S. (1939) *Med. J. Aust.*, **1**, 681

MIGRAINE

See also Vol. VIII, p. 604.

Aetiology

Associated Hypothyroidism

The association of migraine and epilepsy with hypothyroidism is discussed by A. I. Rubenstone, and the author's contention is supported by the case of a mother and 2 daughters, each of whom showed low basal metabolic rates varying from -14 to -25. Administration of thyroid relieved symptoms and raised the basal metabolic rates to normal. The importance is emphasized of taking the basal reading immediately before an attack of migraine. Lowered thyroid function may initiate a cycle in which the bodily processes are slackened, a sluggish mentality develops, and the pulse is retarded. Incomplete combustion results in accumulation of poisonous products, with the precipitation of an attack of migraine. The action of the toxin may be anaphylactic or allergic, and the thyroid may be temporarily stimulated, so that a reading of the basal metabolic rate taken at this time would be false and misleading. The author considered the most feasible of all theories regarding the aetiology of migraine was that which suggested an inherited allergic susceptibility with associated endocrine imbalance.

Rubenstone, A. I. (1938) *Amer. J. digest. Dis.*, **5**, 295.

Treatment

Hypertonic Saline Solution—G. Villey *et al.* cured attacks of migraine by intravenous injection of 20 c cm. of 10 per cent or 20 per cent (hypertonic) solution of sodium chloride, no improvement, however, resulted from such an injection given for headache resulting from cholecystitis. The good effect of these injections may result from diminution of intracranial pressure, or from modification in the colloidal condition of fluids within the skull. Improvement with many treatments was observed in cases of migraine. Perhaps all these produced modification of water metabolism, and as a consequence changed the balance of colloids and of osmosis.

Oxygen inhalation.—W. C. Alvarez has described a new form of treatment for migraine, namely the inhalation of pure oxygen which can be easily given to patients with the help of a new apparatus devised by Boothby, Lovelace, and Bulbulian. Several cases are briefly mentioned in which this treatment was remarkably successful; in 2 cases gynergen (ergotamine tartrate) had previously been tried without benefit. The amount of oxygen employed is 6 to 8 litres per minute. The treatment is also very effective in other types of severe headache.

Instillation of pilocarpine for eye symptoms—K. Grunert published his observations based on over 1,500 cases of migraine in his practice and emphasized the almost universal occurrence of accompanying eye symptoms. The most common of these was insufficiency of accommodation due to muscular weakness. The therapy of this condition by the instillation into the eye of 0.5 per cent pilocarpine, rising to 1 per

cent in the evening, was universally effective. Sometimes it was necessary to repeat this instillation; in prolonged cases, 1 to 2 weeks' treatment with 2 daily doses, rising to 2 per cent in the end, was necessary, and the effect on the patients was very marked. Sunday migraine, the phenomenon feared in busy housewives or office workers, who only had migraine if they stayed in bed longer than usual, always disappeared under this treatment, and another advantage of the therapy was the speed with which the patients went to sleep. Pilocarpine in oil can be used with advantage instead of the instillations. If the eyes reveal other anomalies, glasses must be ordered. Pilocarpine treatment can be continued for long periods, and the patients can hold the oil in readiness to rub in whenever an attack is feared.

Complications of ergotamine tartrate therapy.—T. J. C. von Storch investigated complications following ergotamine tartrate therapy in migraine. Ergotism rarely develops, but accessory symptoms, especially after intravenous administration, are more common. The commonest accessory symptoms are nausea, vomiting, numbness or tingling in the extremities, muscular pains and stiffness, and fatigue. Overdosage is the commonest cause of these ill effects. Contra-indications to the use of the drug are septic states, and obliterative vascular disease, and it should be used with caution in the presence of marked arteriosclerosis and hepatic or renal diseases, vitamin C deficiency, and hypersensitivity to the drug. Forty-two cases of this condition were reported from the literature. It is estimated that they constituted only 0.01 per cent of cases in which ergotamine tartrate was used. No complications were reported following its use in 189 cases of migraine.

J. M. Watt also referred to the untoward effects of ergotamine, the commonest of which are nausea and vomiting which yield to hypodermic injection of atropine sulphate ($\frac{1}{100}$ gr.). Other effects are weakness of the legs, stiffness of joints, constriction of the throat, heaviness in the chest, and burning and tingling of the fingers and toes; for muscular pains an intravenous injection of 10 c.cm. of calcium gluconate solution is advised. The patient should always lie down quickly for 1 to 2 hours after the administration of ergotamine.

Alvarez, W. C. (1939) *Proc. Mayo Clin.*, **14**, 173.

Grunert, K. (1939) *Munch. med. Wschr.*, **86**, 841.

Storch, T. J. C. von (1938) *J. Amer. med. Ass.*, **111**, 293.

Villey, G., Buvat, T. F., and Mmc. Buvat-Pochon (1938) *Rev. Neurol.*, **70**, 32.

Watt, J. M. (1938) *S. Afr. J. med. Sci.*, **3**, 95.

MOUTH DISEASES

See also Vol. VIII, p. 620, and Cumulative Supplement, Key Nos. 1084-1090.

Tongue

Glossodynia

S. S. Greenbaum reviewed 33 cases of glossodynia observed over a period of 12 years. Glossodynia refers actually to a burning sensation of the tongue, although many patients complain also of generalized oral burning, alteration in taste, and dryness or salivation. The condition may last for days or years. The pain may be intermittent or continuous. It represents in the mouth what pruritus is in the skin. According to the author, glossodynia should be classified as essential or functional, symptomatic, and mixed. Underlying causes include irritation, intolerance to drugs or substances in artificial dentures, lingual tonsillitis, anaemia, derangement of the temporo-mandibular joint, or irritation of papillae foliatae by irregular teeth. Slight trauma to the tongue may result in a cancerophobia with all the symptoms of glossodynia, which reassurance will effectively resolve. The author draws attention to the painful form of wandering rash of the tongue (erythema migrans), and points out the necessity of excluding the abortive forms in patients who complain of a more or less localized burning sensation in the tongue.

Epidemic Glossitis

Clinical picture.—I. Katzenellenbogen in Palestine during the last quarter of 1938 observed 24 patients with epidemic glossitis. The swellings of the papillae, mainly of the fungiform papillae, were accompanied by inflammation of the angle of the mouth and by thick coating of the back of the tongue. In 80 per cent of cases

grooving of the tongue was marked, the epithelium between the grooves in cases with frequent relapses being thickened.

Treatment with nicotinic acid.—Of Katzenellenbogen's 24 patients, 21 showed great improvement on the administration of nicotinic acid—the dosage being generally 50 mg., 4 to 6 times a day. The author attributed the glossitis to a deficiency of this element, and thought that the accompanying stomatitis was similar to the condition of the tongue in acute pellagra, though other manifestations of that condition never appeared. The theory advanced some years ago that glossitis was related to the eating of unripe oranges is untenable. To ensure success nicotinic acid must be administered for a long period. Its use gives rise to no discomfort apart from its rubefacient effect.

Greenbaum, S. S. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 686.

Katzenellenbogen, I. (1939) *Lancet*, **1**, 1260.

Tumours

Carcinoma

A. J. Gardham, from analysis of 84 cases of buccal carcinoma, classified them into 3 grades of malignancy. (i) Most carcinomas of the lip and small carcinomas of the cheek were accessible, not highly malignant, and responded well to both surgical measures and irradiation. Regular examination of the neck for metastases was preferable to prophylactic irradiation. (ii) Carcinoma of the floor of the mouth; carcinoma of the epiglottis, and some antral and pharyngeal carcinomas were inaccessible but not highly malignant. These were curable by irradiation unless they had already invaded bone, but considerable damage might be sustained by normal tissue in the process. These 2 grades might be approached surgically by a median incision. (iii) A large proportion of carcinomas of the mouth and infiltrating carcinomas of the lower jaw were highly malignant. Infiltrating carcinomas of the lower jaw were considered separately because it was impossible to impede their growth by radiation without the risk of immediate necrosis of the jaw, it was possible that in these cases, though not in the other buccal carcinomas, an extensive operation might prove effective. Operations in the buccal carcinomas were extensive, mutilating, and seldom justifiable. In cases obviously malignant, as shown by the early appearance and rapid spread of metastases, surgical procedure might accelerate rather than retard the spread of the tumour. Even small lesions, resistant to adequate interstitial irradiation, should not be subjected at once to extensive supposedly radical operations; diffuse recurrence was prone to occur, and diffuse recurrence was a worse fate than death from an untreated carcinoma. Probably the best treatment for these small but very malignant carcinomas was a localized diathermy excision. Temporary improvement might be obtained by irradiation without any alteration of the ultimate prognosis, but was unlikely to do harm and in this respect was far preferable to operation.

In the pain during the later stages of carcinoma of the tongue, maxilla, or of the nasopharynx even after surgical intervention or irradiation, W. Harris advocated the injection of the Gasserian ganglion with alcohol when the 5th cranial nerve is involved. Great relief was obtained after a well-placed injection which dispensed with the need for resection of a sensory root or a trigeminal tractotomy. The lateral route of approach was most generally employed. In carcinoma of the tongue, considered inoperable owing to its invasion of the floor of the mouth or because it has recurred after the operation or radium treatment, a less extensive injection of the 3rd division of the trigeminal at the foramen ovale will anaesthetize the area of the disease and relieve pain without the necessity of pushing the needle on into the Gasserian ganglion.

Gardham, A. J. (1939) *Lancet*, **1**, 677.

Harris, W. (1938) *Brit. med. J.*, **2**, 831.

MUMPS

See also Vol. IX, p. 1.

Morbid Anatomy

V. de Lavergne *et al.* described the histological changes in the parotid in mumps in order to decide whether the infection was ascending or descending. The old

opinion was that the changes were interstitial vasodilatation, oedema, and mononuclear infiltration. Later, biopsies in man (4 cases) and in monkeys by Johnson and Goodpasture added infiltration around the ducts and blood vessels, and degeneration in the cellular secreting epithelium, the latter lesion being contested by others. The resemblance of the microscopical appearances to those in rabies were so striking as to make it highly probable, though not finally proved, that a neurotropic ultravirus reached the parotid by the nervous route.

Johnson, C. D., and Goodpasture, E. W. (1936) *Amer. J. Path.*, **12**, 495.

de Laveigne, V., Kissel, P., and Leichtman, P. (1939) *Pr. méd.*, **47**, 757.

Complications

Meningitis

W. Schoenfeld held the view that epidemic parotitis is not often the presenting condition in general practice. Patients usually present themselves with another clinical syndrome and in course of the examination the condition is revealed. Acute pancreatitis, enlargement of the thymus and the thyroid, and otitis or midocyclitis and other ophthalmic conditions prompt the patient to seek medical advice. All these conditions can be and often are due to epidemic parotitis. The author reported 4 cases in which the central nervous system was involved together with epididymitis. Lumbar puncture revealed a latent meningitis in all 4 cases, the meningitic process bearing a marked resemblance to the meningitis often coupled with herpes zoster. The condition is usually mild, and the patient can be easily cured by rest. The author expressed his view that this complication occurs more often than is usually believed.

Schoenfeld, W. (1939) *Munch. med. Wschr.*, **86**, 880.

MUSCLE DISEASES

See also Vol. IX, p. 11, and Cumulative Supplement, Key Nos. 1093-1099.

Muscular Dystrophies

Pseudo-hypertrophic Muscular Dystrophy

Pancreatic dysfunction—L. Scheman *et al.* quote the work of Meldolesi who, having investigated 100 cases of pseudo-hypertrophic muscular dystrophy, thought that the condition was due to a primary disease of the pancreas in which tryptic and lipolytic digestive processes were impaired. Protein was not properly absorbed, and there was a consequent depletion of protein reserves resulting in dysplasia of striated muscle. Persons concerned showed a hereditary lack of muscular pigment. A diminished dextrose tolerance was present in some cases, and the total nitrogen excretion was low. Meldolesi treated these cases with 40 to 60 min. of Richter's pepsin-pancreatin twice a day, with insulin, and with intravenous dextrose. L. Scheman *et al.* investigated 5 patients with a history of pseudo-hypertrophic muscular dystrophy from the age of 6, and the examination of the stools, duodenal contents, and urine furnished no evidence that the pancreas was functioning abnormally in this disease. Specific treatment with pancreatin did not influence the muscular condition.

Progressive Muscular Dystrophy

Creatine metabolism—R. Stahli discusses the hypothesis of Ken Kuré concerning the fourfold innervation of muscles and K. Thomas's observations on the creatine metabolism in progressive muscular dystrophy. According to Ken Kuré any damage to the autonomic nervous system may lead to a myopathy. Thomas is of the opinion that an increased creatine excretion is characteristic of progressive muscular dystrophy. The author describes the case of a man suffering from progressive muscular dystrophy after injury of the spinal column. The symptoms were characteristic, but there was no hypercreatinuria. His conclusion is therefore that progressive muscular dystrophy can occur without hypercreatinuria, and that the latter symptom is not a cause of progressive muscular dystrophy. According to Netrolitzky and Pichler, in some cases there is a definite clinical improvement without any change in the hypercreatinuria, and in some cases the hypercreatinuria improved without any increase of muscular strength.

Treatment with glycozell.—S. Pastinsky reported the appearance, in a number of systemic nervous diseases, of ulcers of the leg which were always very resistant to usual methods of treatment. He published an observation on the improvement of such a torpid ulcer which occurred in the course of a progressive muscular dystrophy on treatment with glycozell. The mechanism of the efficacy of glycozell in muscular dystrophy is not yet known, and the author suggested that the nutritive action of glycozell on the atrophic musculature was responsible for the curative effect in ulcers of the leg. The observation has further shown the relation between a systemic nervous process and its effect on the skin.

Carbohydrate Metabolism

D. Pallikan reports experiments designed to discover whether disturbance of carbohydrate metabolism was a constant symptom of myopathy, and whether alteration in carbohydrate metabolism was a specific sign of myopathy. In 8 cases of myopathy and in 16 normal controls 1 c cm. of adrenaline solution was injected into a muscle, the carbohydrate and lactic acid content of the blood were examined while the effect of the adrenaline lasted. The excretion of creatine on the days preceding injection, and on the day following, was compared. The result was as follows: (i) Carbohydrate in the blood was not significantly abnormal in a case of myopathy. (ii) The adrenaline-lactic acid curve was also normal in most cases. In 4 cases of myopathy the maximal concentration of lactic acid was delayed; this was never observed in the controls. The lactic acid curve was very flat in one case, the result of a severe infection. After an injection of adrenaline, creatinuria was increased in every case of myopathy, either on the day of injection or on the next day. This also occurred in healthy control cases, so that this sign also was not characteristic of myopathy.

Netroitzky, P., and Pichler, F. (1938) *Wien Arch. inn. Med.*, **32**, 121.

Pallikan, D. (1939) *Z. ges. Neurol. Psychiat.*, **166**, 236.

Pastinsky, S. (1939) *Munch. med. Wschr.*, **86**, 818.

Scherman, L., Lewin, P., and Soskin, S. (1938) *J. Amer. med. Ass.*, **111**, 2265.

Stahli, R. (1938) *Schweiz. med. Wschr.*, **68**, 1226.

Myotonia Congenita (Thomsen's Disease)

Differential Diagnosis

Opinions differ as to whether myotonia congenita, myotonia atrophica, and paramyotonia are one and the same affection or fundamentally different. Myotonia was observed by O. Maas and A. S. Paterson in nearly all the muscles of cases in myotonia atrophica as well as in cases of myotonia congenita. Pseudo-hypertrophy also was observed in both affections. Wasting, the most characteristic sign of myotonia atrophica, may be extremely mild, even in a case of long duration. Weakness and abolished or diminished reflexes were observed in myotonia congenita as well as in myotonia atrophica. Also other signs did not permit the conclusion that there is a real difference between these affections. Both often start in infancy; it is an error to maintain that dystrophia myotonia starts later than myotonia congenita. A few cases diagnosed 'myotonia congenita' at an early age were examined later, and it was observed at this second examination that signs of myotonia atrophica had developed. Paramyotonia is only a slight variant. True myotonia acquisita is an affection *sui generis*.

Treatment

Quinine sulphate—W. A. Hawke reported a case of myotonia congenita in a boy aged 7 treated with 5 gr. of quinine sulphate 3 times a day. Headache and enuresis supervened, so that the drug was discontinued, return of symptoms then followed. When treatment by quinine was resumed, 10 gr. 3 times a day brought so much relief that this treatment was continued for 9 months.

Action of quinine.—G. Briscoe conducted experiments to determine whether the depressant effects of prostigmin in normal muscle were antagonized by quinine as they were by curarine, and found that, injected intravenously, quinine was antagonistic to prostigmin and synergistic with curarine. Muscular contractions were recorded with a flat steel spring held in a steel frame. Quinine may produce its effect: (i) by reducing the excess of acetylcholine from a depressant level to the level for normal excitation; (ii) by raising the threshold of the motor end-plates, and (iii) by direct action on the muscle fibres. If quinine acts like curare, the first explanation

may be correct. In myotonia congenita the effect of quinine may be either (ii) or (iii), but without knowing the cause of the disease it is difficult to decide which is more important. In myotonia the author considered that there was hyperexcitability to normal amounts of acetylcholine, in contrast to eserine depression in which there is normal excitability to abnormal amounts of the transmitter.

Briscoe, G. (1939) *Lancet*, **1**, 1151.

Hawke, W. A. (1938) *J. Pediatr.*, **13**, 236.

Maas, O., and Paterson, A. S. (1939) *Brain*, **62**, 198.

Myotonia Atrophica

Actiology

Heredity—F. Katzenstein-Lutro examined 2 families affected by myotonia atrophica. They had in common one great-grandfather who suffered from senile cataract. Inheritance in these families was always through the males. Some persons suffered from a *forme fruste* in that generation in which other persons were affected by all signs of the disease. Some children at the age of 11 and 14 years were affected by typical signs of myotonia atrophica. Several persons suffered from a goitre. Members of these families affected by myotonia atrophica were also affected by abnormality of intelligence and affect; many also by abnormality in teeth and in upper and lower jaws. Inheritance in this condition takes place in an irregular dominant manner. Improvement in physical and mental signs was observed in some members of these families who could be examined repeatedly during several years.

A. Ravin and J. T. Waring examined 33 members in 4 families, 12 persons with myotonia atrophica were examined, and the affection was reported in 4 other cases. Direct transmission from parent to child was observed, the children being affected at an earlier age than the parents. This disease is transmitted by a single dominant factor, but the dominance is modified by the occurrence of progressive inheritance (anticipation and potentiation in later generations). The children tend to develop the disease early enough to prevent further propagation. Fraternal anticipation, i.e. earlier onset in the younger siblings of a sibship, was also observed.

Clinical Picture

Disturbance of vibration sense—By the use of an electromagnetic vibrator constructed by Newman and Corbin, O. Maas observed disturbance of vibration sense in the majority of cases of myotonia atrophica, in mild as well as in marked cases. Other signs of disturbed sensibility were observed less often. They occur, however, in a sufficient number of cases to make it unlikely that they are the result of any affection complicating myotonia atrophica. The frequency of signs of sensory change in myotonia atrophica suggests that this condition is not solely the result of an affection of the muscles.

Katzenstein-Lutro, E. (1938) *Schweiz. Arch. Neurol. Psychiat.*, **42**, 249.

Maas, O. (1938) *Brain*, **61**, 449.

Ravin, A., and Waring, J. T. (1939) *Amer. J. med. Sci.*, **197**, 593.

Dystonia Musculorum Deformans

Treatment

Quinine—A case was reported by G. B. Hassin of a girl aged 8 who came for examination exhibiting violent and grotesque muscular movements of the neck, trunk, and extremities. The body was doubled up, the head being drawn over the chest. Extreme restlessness, heavy breathing, and palpitations were present, the only position which afforded any relief being a genu-pectoral posture in which the patient lay on her abdomen with knees flexed and the head resting on the hands. A diagnosis of dystonia musculorum deformans was made. The author considered that the motor restlessness in this condition was probably a disturbance of muscle tone with some secondary neuro-histological changes due to physio-chemical factors similar to those present in myotonia congenita—Thomsen's disease. He therefore considered that quinine, which is effective in that condition, would be likely to control the anomalous muscular contractions in dystonia musculorum deformans. Dosage was commenced with 1 gr. of quinine sulphate, 3 times a day, and increased later to 5 gr., 3, 4, or 5 times a day. Ten months later the patient's condition was very satisfactory except for the laborious nature of her gait. The maintenance dose

had been established at 10 gr. daily. The particular interest of this case lay in the unusually early onset of the disease, at 16 months, and the postural anomalies which were the only clinical manifestations persisted even when the muscular restlessness was so much improved. Two other patients responded to quinine therapy, one aged 6 and exhibiting a spasmodic torticollis. The dosage in the latter case was as high as 30 gr. per day.

Hassn, G. B. (1939) *J. Amer. med. Ass.*, **113**, 12.

Creatine Metabolism in Various Muscle Diseases

Creatinuria and diminished excretion of urinary creatinine are common findings in patients with muscular wasting following disease of the nervous system. A. T. Milhorat and H. G. Wolff investigated the metabolism of creatinine and creatine in 17 patients with muscular wasting due to various conditions. They found that the diminution in the output of creatinine was directly proportional to the reduction in muscle mass. The amount of creatine eliminated was smaller than in patients with progressive muscular dystrophy with similar amounts of apparent wasting but, if the muscular wasting was extensive enough to include most of the skeletal muscles, the diminution equalled that seen in advanced cases of progressive muscular dystrophy.

The same authors, in a later paper, studied the factors influencing creatine and creatinine metabolism in myotonia congenita, myotonia atrophica, amyotonia congenita, and dystonia musculorum deformans. They also determined the effect of muscular activity (tremor) on the output of creatine and creatinine. In patients with myotonia congenita, the excretion of creatinine was similar to that of normal persons of the same weight, sex, and muscular development. Patients with dystonia musculorum and paralysis agitans were found to have no obvious impairment in the metabolism of creatine and creatinine. Tremor had no effect on the elimination of creatinine and creatine, or on the creatine tolerance. There was diminution in the excretion of creatinine directly proportional to the reduction in muscle mass in patients suffering from myotonia atrophica. Patients with amyotonia congenita excreted large amounts of creatine, and their creatine tolerance was low. Ingestion of aminoacetic acid increased the amount of creatine excreted and further reduced the tolerance. The output of creatinine was greatly diminished.

Milhorat, A. T., and Wolff, H. G. (1938) *Arch. Neurol. Psychiat.*, *Chicago*, **40**, 663, 680

MYASTHENIA GRAVIS

See also Vol. IX, p. 34.

Clinical Picture

The possibility of the development of a psychiatric syndrome during the course of myasthenia gravis is described by R. T. Collins. He recorded 2 such cases, the first of which was admitted to a mental hospital with a diagnosis of psychoneurosis, and the second because he had become impossible to manage in the open ward of a general hospital. The first responded well to sympathetic handling combined with prostigmin therapy. The second, which proved to be a psychosis with great psychomotor activity, though treated with prostigmin, atropine, and ephedrine, succumbed to a respiratory crisis on the sixth day.

Collins, R. T. (1939) *Brit. med. J.*, **1**, 975.

Treatment

Prostigmin

D. P. H. Schafer treated a case of myasthenia gravis with prostigmin, commencing with intramuscular injections of 2 c cm. Later, oral treatment was instituted, and in this case one 15 mg. tablet, 5 times a day, was found to be the maintenance dose. The midday and afternoon tablets were accompanied by a benzedrine tablet. The author stated that 30 mg. of prostigmin given orally was equivalent to 0.5 mg. given parenterally, and the oral dose might vary in different cases from 4 to 12 tablets of 15 mg. per day. Any gastric or intestinal disturbances which occurred during the period when dosage was being established were controlled by the addition

of 0.3 mg. of atropine sulphate given in conjunction with the prostigmin. The patient showed considerable improvement under this treatment. She could smile and close her eyes normally and swallow without difficulty or regurgitation. She gained 13 pounds in weight in 12 weeks, and stated that she felt perfectly well.

Schafer, D. P. H. (1939) *Med. J. Aust.*, **1**, 730

MYIASIS

See also Vol. IX, p. 58, and Cumulative Supplement, Key Nos. 1104-1109

Larva Migrans

Clinical Picture

N. I. Murray investigated cases of 'creeping eruption' in adults to discover the causal organism. A dissecting microscope, some cedar wood oil, and a sharp eye-spud were used to focus the thin inflammatory track which is characteristic of this condition. The obvious track is about 3 mm. wide but the true track is only one-tenth of that width until sepsis arises. By using the eye-spud, the track was exposed right to its terminus. The drops of fluid in the burrow are transferred to the slide and the latter is examined under the microscope. In 30 tracks examined, no evidence was found of the presence either of a fly larva (*Gastrophilus* or *Hypoderma*) or of a larval dog-hookworm (*Ankylostoma braziliense*). A number of slides in one case revealed a mite about 300 μ in length and 2 developmental stages. In a second, a similar mite with a number of eggs was found. The eggs were a little larger than polymorphonuclear leucocytes. The nearest resemblance shown by this mite is to *Tetranychus molestissimus*, which is found in the Argentine and Uruguay on the under-surface of the leaves of *Aanthum macrocarpum*. It attacks man, and is characterized by pruritus and pyrexia.

Murray, N. I. (1939) *Brit. med. J.*, **1**, 1026

MYXOEDEMA

See also Vol. IX, p. 69

Aetiology

B. Castleman and S. Hertz collected 6 cases of pituitary fibrosis with myxoedema, and regarded the primary change and responsible factor as being in the anterior lobe of the pituitary, and the atrophy of the thyroid, parathyroids, adrenals, ovary, and uterus (in their case) as secondary. There was no cachexia, but otherwise the condition resembled Simmonds's disease. In their case the thyroid was extremely fibrotic.

Castleman, B., and Hertz, S. (1939) *Arch. Path.*, **27**, 69

Morbid Anatomy

Gonads in Myxoedema

D. Marine examined microscopically the testes of a man, aged 63, and found that the interstitial cells were atrophied; this appeared to be the first observation on a case of ordinary myxoedema, though a case of myxoedema after thyroidectomy (cachexia thyroopriva) had been reported by Wegelin, who examined the testes, which were hypoplastic, microscopically but did not mention the condition of the interstitial cells.

Marine, D. (1939) *Arch. Path.*, **25**, 65

Wegelin, C. (1925) *Vuchows Arch.*, **254**, 689

Clinical Picture

Atypical Syndromes

E. Rose points out that, in addition to the classical picture of myxoedema, there are various atypical forms in which the symptoms may not be recognized as due to thyroid deficiency. Among these may be mentioned amenorrhoea and sterility, a mild hypochromic anaemia; glossitis and pellagra; coronary sclerosis and cardio-

vascular manifestations; abdominal pain and ascites both of which are very rare; retention of urine; and neuropsychiatric disorders. In addition, rare cases of true primary anaemia may occur simultaneously with myxoedema. Atypical hypothyroidism in childhood may be diagnosed by X-ray evidence of delayed bony development. Blood cholesterol is also increased. A group of cases exists in which the symptoms are almost completely the reverse of the classical picture, with the exception of sensitivity to cold and the tendency to be easily fatigued. This type is described as suffering from paradoxical hypothyroidism. These various types of atypical myxoedema all respond well to thyroid therapy, the dosage being adapted to individual needs. A different problem is presented by a group who present typical hypothyroid symptoms, which are not caused by a genuine thyroid deficiency, and do not respond to thyroid treatment. A valuable diagnostic aid is the absence of hypercholesterolaemia. Such patients have been successfully treated with benzedrine sulphate or ephedrine.

Hypertrophy of Muscles

P. Mallaret and J. Sigwald described the case of a man of 51 who developed generalized hypertrophy in all his muscles with some oedema but without diminution in strength. The thyroid was somewhat reduced. Myotonia on mechanical excitation was observed only in a few fibres of the biceps. The patient was cured by administration of thyroid. The authors discussed more or less similar cases previously described in which muscle hypertrophy, diagnosed as true hypertrophy or as pseudo-hypertrophy, was combined with more or less definite signs of myotonia. The authors thought it probable that thyroid deficiency was the cause of the muscle disturbance.

Mallaret, P., and Sigwald, J. (1939) *Rev. neurol.*, **71**, 513.

Rose, E. (1939) *Penn. med. J.*, **42**, 752.

NAILS, DISEASES OF

See also Vol. IX, p. 83

Absence of Thumb Nails

H. H. Strandkov reported 4 cases in 3 generations of absence of the nails of the thumbs, but without the concomitant absence of the patellas recorded in the previous pedigree of absent thumb nails (Osterreicher) and in a case of absent patellae (Little).

Little, I. M. (1897) *Lancet*, **2**, 781.

Osterreicher, K. (1939) *Wien klin. Wschr.*, **42**, 632.

Strandkov, H. H. (1939) *J. Hered.*, **30**, 53.

Paronychia

Morvan's Disease

Morvan's disease, a painless paronychia described by Morvan in 1853, was for many years regarded as a special disease. Joffroy and Achard observed painless paronychia in cases of syringomyelia in 1890, and shortly after painless paronychia was also observed in cases of leprosy. Since that time 'Morvan's disease' has been regarded as a sign either of syringomyelia or of leprosy. R. Cruchet and P. Delmas-Marsalet observed a case of acrodynia in which trophic disturbance producing painless paronychia was considered to be due to lesions of the sympathetic spinal centres. They therefore considered that the signs observed by Morvan may also result from acrodynia. They suggest the name 'Morvan's syndrome' instead of 'Morvan's disease', as a chronic destructive lesion in the sympathetic centres of the spinal cord resulting from various causes may produce the symptoms described by Morvan.

Cruchet, R., and Delmas-Marsalet, P. (1939) *Conf. Neurolog.*, **2**, 32.

Primary Carcinoma of the Nails

J. Levine and J. R. Lisa, report a case of primary carcinoma of the nails, a rarely recorded condition, and analyse the 17 proved cases and one probable example. In these 19 cases 11 were males, 7 females, and in one the sex was not given; the

extremes of age were 21 and 75 years; in 10 cases there was a history of injury often followed by chronic infection; the hand was the site of the tumour in 13 cases, and in 9 of these the right thumb or index finger was attacked; in 6 cases the disease occurred in the great or the small toe. In 2 cases the carcinoma was basal-celled, in one an early carcinoma arose in a papilloma, but the most frequent was a squamous-celled carcinoma of low malignancy. In 7 cases pain was the prominent symptom. Excision was followed by good results except in 2 cases, one with metastases in the lymphatic glands, and the other with a local recurrence after treatment by X-rays.

Levine, J., and Lisa, J. R. (1939) *Arch. Surg., Chicago*, **38**, 107.

NARCOSIS, PROLONGED

See also Vol IX, p 98, and Cumulative Supplement, Key No. 1118

Medinal and Luminal

R. S. Wilson and S. W. Gillman treated a series of cases in a mental hospital by prolonged narcosis which was induced by a combination of medinal (soluble barbitone) and luminal (phenobarbitone). The list comprised 32 cases of melancholia; 10 of mania, 7 of schizophrenia, 5 with anxiety hysteria, and one epileptic. The mixture contained 5 gr. of medinal and one gr. of luminal in each fluid drachm. The dosage was 2 fluid drachms every 4 hours until sleep was induced, and one fluid drachm thereafter as required. It was found that, although in some cases grave complications arose, these were less frequent than in somnifaine narcosis. The results were considered as good as those obtained in the latter treatment, but not so dramatic. The best results were in mania. In melancholia they were good, but in schizophrenia the treatment was ineffective. The treatment of epileptic psychosis by this therapy is contra-indicated, and was associated with the only death in the series.

Wilson, R. S., and Gillman, S. W. (1938) *J. ment. Sci.*, **84**, 991

Dangers

In addition to the 50 known complications of sleep treatment, a previously unrecognized one, namely thrombophlebitis due to barbiturates, has been recorded by H. A. Palmer. In 150 cases thus treated there were 4 cases, 3 of thrombophlebitis of one lower limb, and one of cerebral thrombosis. Three of the men, about or past the border-line of age-safety (55), were given a very much modified form of treatment. It is suggested that every patient undergoing sleep treatment should be given a small dose of potassium citrate, and, in addition to daily exercises, should receive a little vigorous massage to the lower limbs.

Palmer, H. A. (1939) *J. ment. Sci.*, **85**, 276

NECK: TUMOURS AND OTHER MORBID CONDITIONS

See also Vol IX, p 104

Tumours

Metastatic Carcinoma

Complete excision of the lymphatic glands of the neck for malignant disease was undertaken by L. C. Cohn in 31 cases between the years 1925 and 1937. One or more glands were palpable before operation and all cases were subsequently verified by histological examination. The majority of the cases were secondary to carcinoma of the tongue. The operative mortality for the series was 10 per cent. The results of pre-operative irradiation were usually not of sufficient value to delay operation. Many of the patients remained free from carcinoma, and this extensive operation should therefore be undertaken in operable cases.

Cohn, L. C. (1938) *Arch. Surg., Chicago*, **37**, 240.

NEPHRITIS AND NEPHROSIS

See also Vol IX, p 134, and Cumulative Supplement, Key Nos 1131-1141

Morbid Anatomy*Acute Nephritis*

A. E. Feller and H. M. Hurevitz reported 2 clinical cases of acute nephritis with cardiac failure, one of which had a wide-spread inflammatory lesion of the arterioles including those of the heart, with minimal glomerular change. Necropsies of the 2 cases revealed arteriolar changes in the striated muscle, haemorrhages in the ocular fundi, haematuria, hypertension, and cardiac failure. The necropsy findings suggest the probability that both cases were suffering from the same disease. It was therefore suggested that acute nephritis might be part of a wide-spread vascular lesion—panarteriolitis, and that in many patients with acute nephritis and cardiac failure the underlying cause was panarteriolitis with involvement of the vessels of the myocardium. Although not mentioned in the paper the conception of renal disease as a local manifestation of generalized arterial disease appeared in F. E. Klein's report on the wide-spread microscopical changes in the blood vessels in scarlet fever. W. W. Gull and H. G. Sutton had previously put forward their well-known view of arterio-capillary fibrosis as a general vascular change responsible for the chronic interstitial (arteriosclerotic or ischaemic kidney) nephritis.

Feller, A. E., and Hurevitz, H. M. (1938) *Amer. Heart J.*, **16**, 568.

Gull, W. W., and Sutton, H. G. (1872) *Med.-Chir. Trans.*, **55**, 273.

Klein, F. E. (1876) *Report of the Medical Officer of Privy Council and Local Government Board*, N.S., No. 8.

Clinical Pathology

F. N. Allott has observed several patients who, although free from renal disease, showed a high level of sodium and chlorine in the serum, and a high blood urea. The sodium and chlorine figures in the urine were low, and the potassium, phosphate, and sulphate figures high. All the patients, except one who did not have a necropsy, revealed a lesion in the central nervous system, but this was varied in type. The author thought that the changes in the sodium and chlorine might be explained by a reabsorption up to a certain maximal quantity by the renal tubules. Alternatively he thought that there might be an abnormality in the nervous or glandular renal control.

Nephrosis

Basal metabolism—L. I. Farr measured the basal metabolic rate in 8 children with the nephrotic syndrome. The ideal weight rather than the actual weight of the oedematous child was used in calculating the surface area of the body, since the retained salt and water play no part in the consumption of oxygen. In no case was there a consistently lowered basal metabolic rate, in one case a consistently slightly elevated rate was noted.

Complement Activity of Blood

C. I. Kellett and J. Greig Thomson, in the course of a 3-year investigation into the subject of complement activity of the blood, made more than 400 estimations of serum from various conditions with an average of about 85 per cent. This was part of the present investigation into the complement titre of the blood in nephritis. The 38 cases of nephritis were divided into acute, subacute, chronic, and doubtful forms of nephritis. It was found that all the cases of acute glomerulonephritis, examined within 4 weeks of the onset, showed a remarkably deficient titre of complement, which in the seventh week from the onset returned to normal. In no other form of nephritis was the deficiency of complement found. It might therefore have a diagnostic value. Deficiency of complement was noted in 1901 (Neisser and Doering), and was regarded as pathognomonic of uraemia until this was refuted in 1904 by H. Senator, and since then the subject appeared to have fallen into ill-deserved neglect and been forgotten.

Allott, F. N. (1939) *Lancet*, **1**, 1035.

Farr, I. E. (1938) *Amer. J. Dis. Child.*, **56**, 309.

Kellett, C. I., and Thomson, J. G. (1939) *J. Path. Bact.*, **48**, 519.

Neisser, I., and Doering, H. (1901) *Berl. klin. Wschr.*, **38**, 593.

Senator, H. (1904) *Berl. klin. Wschr.*, **41**, 181.

Course and Prognosis

Acute Glomerulo-Nephritis

A series of 10 cases of glomerulo-nephritis is divided by E. N. Loeb *et al.* into 2 groups of 8 and 2 respectively, and discussed in reference to the permanence of recovery. It is shown that no case of healed acute glomerulo-nephritis has subsequently developed chronic progressive renal disease, in spite of recurrent haemolytic streptococcal infection. Eight of the patients whose nephritis at onset was preceded by haemolytic streptococcal infection were observed through healed periods varying from 8 months to 3 years. In each case the supervention of a haemolytic streptococcal infection produced no recurrence of the nephritis. The other two patients, observed through corresponding periods of 10 months and 10 years respectively, underwent an infection. In the first this was proved to be caused by haemolytic streptococci, and in the second it was presumed that it was caused by these organisms. Both patients developed transient gross haematuria, but no significant albuminuria.

K. H. Tallerman and J. H. Burkinshaw continued a follow-up study of 16 out of 25 patients who had had an attack of acute nephritis in the 3 years 1927 to 1929. Of the other 9 patients 7 could not be traced and the remaining 2, who were unable to attend by reason of their employment, appeared perfectly fit. The 16 cases showed, (a) complete recovery in 5, (b) recovery in 8, (c) a probably complete recovery in one case, and (d) two patients with a trace of albuminuria and an impaired excretion of phenolsulphophthalein with diminished urea-concentration who must be considered examples of 'renal damage'. In the second group, findings were normal, but albumin was present. In 4 females over the age of 12 the albumin may have been vaginal rather than renal in origin and, if this had been verified, these should have belonged to class (a).

A. W. Snoke at the Rochester Medical School followed up 146 children, from one to 15 years of age, who had been diagnosed as cases of glomerulo-nephritis, on the basis of the finding of red blood-cells, albumin, and casts in the urine. The follow-up periods varied from one to 9 years. Of the patients 72.6 per cent had completely recovered, 14.2 per cent had active lesions, and 13.2 per cent were dead. These figures are much more favourable than those in a similar series studied at Stanford University. Climatic factors may partially explain this, together with the fame of Dr. Addis which would attract more severe cases to San Francisco.

Loeb, E. N., Lyttle, J. D., Seegal, D., and Jost, E. L. (1938) *J. clin. Invest.*, **17**, 623.

Snoke, A. W. (1939) *Amer. J. Dis. Child.*, **57**, 1373.

Tallerman, K. H., and Burkinshaw, J. H. (1939) *Lancet*, **1**, 1255.

Complications

Nephrosis

C. A. Aldrich and H. H. Boyle treated the pneumococcal peritonitis (the peritoneal syndrome) complicating nephrosis with 40 to 100 c.cm. of either erysipelas or scarlet fever convalescent serum. Previously this condition had been responsible for a 90 per cent mortality, whereas in this series of 22 cases there were 5 deaths or 23 per cent only. Patients with erysipelas-like cutaneous lesions all recovered after the serum treatment. It was suggested that either the convalescent serum had a non-specific beneficial effect on other diseases or that the intravenous injection of normal serum influenced the nephrosis favourably and helped the patient to overcome the peritonitis.

Aldrich, C. A., and Boyle, H. H. (1938) *Amer. J. Dis. Child.*, **56**, 1059.

Treatment

Diffuse Haemorrhagic Glomerulo-Nephritis

Amidopyrine. G. Weitzmann tried to find a drug which would shorten the duration of inflammation and healing in diffuse haemorrhagic nephritis. The usual treatment of the disease nowadays consists of dietary measures and physical therapy (diathermy, hot packs). Nephritis occurs very often after angina, scarlatina, and erysipelas. This fact and the occurrence of symptoms such as fever, leucocytosis, and increased sedimentation rate suggested to the author that nephritis might be regarded as a 'rheumatic' disease mainly affecting the renal apparatus. In consequence he tested pyramidon (amidopyrine) in the treatment of nephritis. He treated

16 cases and had 24 control cases. He started giving pyramidon in doses of 0.2 to 0.3 g., 3 to 5 times daily. The haematuria disappeared, and, when the pyramidon treatment was stopped, began again. If pyramidon treatment was continued, the haematuria completely disappeared. Later the doses were increased from 0.3 g. twice a day to 0.2 g. 5 times a day in children, and 0.5 g. 3 to 4 times a day in adults. No by-effects or complications were observed. Whereas haematuria disappeared completely in all of the 16 patients treated with pyramidon, 3 patients of the 24 controls were not completely cured of their haematuria, even after prolonged stay in hospital. The average stay in hospital of the pyramidon patients was 71 days, and that of the controls 78 days.

Weitzmann, G (1938) *Med. Welt*, **12**, 1843

NEURALGIA, GLOSSOPHARYNGEAL AND TRIGEMINAL

See also Vol IX, p 174.

Trigeminal Neuralgia

Treatment

Old tuberculin — C Charlin examined 50 cases of facial neuralgia, 5 only were completely free from signs of tuberculosis, and had never suffered from tuberculosis in any way. All these cases were treated by injection of Koch's old tuberculin. Local and general reactions were observed in some patients who received a relatively

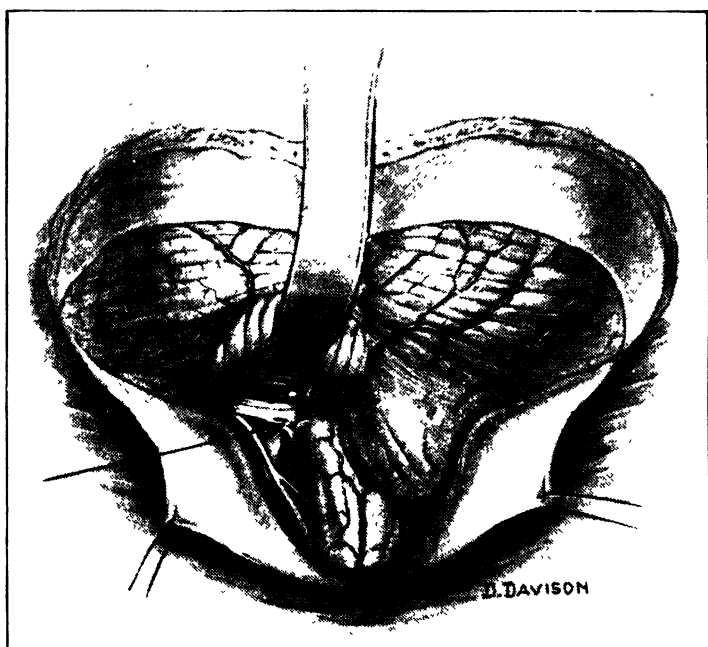


FIG. 18 Showing the site of the incision of intramedullary tractotomy (Rowbotham) (from *British Medical Journal*, 1938)

strong dose. The optimal dose produced analgesia, this dose was repeated several times, and increased later. Weekly injections were given for 2 months. Thereafter no injection was given unless a relapse of the neuralgia developed. Then, a new series of injections was given. Most of the cases affected by facial neuralgia were cured.

Surgical.— G F Rowbotham reported 3 cases in which severe supra-orbital pain

was relieved by section of the pain fibres in the descending tract of the trigeminal nerve. Sjoqvist divided the pain fibres in the descending limb of the trigeminal tract by an incision through the postero-lateral aspect of the medulla oblongata, thus preserving tactile sensation so that the face is not unpleasantly numb. Under avertin and gas and oxygen anaesthesia, a wide cerebellar exposure was followed by the removal of the posterior margin of the foramen magnum, and the dura mater was opened by a Y-shaped incision; the cerebellar lobe was then lifted up so as to expose the restiform body, the roots of the vagus, the curve of the vertebral artery, and the ascending root of the spinal accessory nerve (see Fig. 18). A transverse incision was made into the right tuberculum cinereum 2 mm. above the lowest vagal root and starting close to its origin from the medulla in its outer part for a distance of 4 mm. and to a depth of 3.5 mm. The flaps of dura mater were sewn together to prevent blood from trickling into the posterior fossa from the raw surface of the muscles. The usual careful closure was made in layers. The advantages of the method are that the face is not completely denervated, analgesia is densest in the forehead, and the muscles of mastication are never paralysed. Moreover the great superficial petrosal nerve (nerve of tear secretion) is far from possible injury, and so a dry eye is avoided. The section of the nerve furnishes, for the first time, experimental proof that fibres conveying the various forms of sensation are rearranged within the brain-stem into physiological groups, the pain fibres probably having the lowest and the touch fibres the highest representation in the somatic sensory nucleus of the trigeminal nerve.

Charlin, C. (1938) *Ann. Oculist., Paris*, **175**, 894.

Rowbotham, G. L. (1938) *Brit. med. J.*, **2**, 1073.

NEURITIS

See also Vol. IX, p. 182

Multiple Neuritis

Aetiology

After serum therapy — A. I. Bennett discussed the complication of neuritis following prophylactic and therapeutic injection of antitoxic sera. About 115 cases have been reported, 70 of them in France. The complication usually followed the prophylactic use of tetanus antitoxin but any type of horse serum might be responsible. Almost all cases have been reported in adults, the commonest age of incidence being 26. It appeared at the height of the serum disease, usually one week after the injection. Although cerebral, meningeal, and spinal lesions occurred, the commonest involvement was in the peripheral nerves, the nerves from the cephalic part of the brachial plexus (5th and 6th cervical roots) commonly being affected and producing the characteristic Erb-Duchenne scapulo-humeral palsy. The neuritic type of pain is characteristic, and early diagnosis was easy. Perineural urticaria and oedema compressing the nerve-trunks for a few hours was the probable cause of the palsy. This oedema might occur in the intervertebral foramina, bony grooves, or perineural sheaths of the roots or nerves, interfering with the blood supply and causing anoxaemia with temporary nerve-cell and nerve-fibre death. The anterior-horn motor neurons must be unaffected, because complete regeneration usually occurs. The only sure prophylaxis would be the substitution of serums of other animals for horse serum. The development of tetanus immunization by albumin-precipitated toxoid would eliminate most complications. Adequate early treatment of the neuritis with an abduction splint and complete rest of the arm was recommended. Other methods available were intravenous injection of hypertonic dextrose or blanket sweat-packs with pilocarpine in order to dehydrate muscle, joint, and neural structures, and repeated injections of adrenaline to restrict the amount of nerve damage. The prognosis for recovery within 6 months was good, but about 20 per cent of patients were left with residual weakness and atrophy. The cases are of considerable medico-legal interest since a large percentage develop as the result of treatment administered for an accidental wound and have to be compensated. Great care in the prophylactic administration of antitetanus serum and avoidance of the use of antitoxins not of proved specific value (antistreptococcal or antigonococcal) is strongly advocated.

Bennett, A. E. (1939) *J. Amer. med. Ass.*, **112**, 590.

NEUROFIBROMATOSIS

See also Vol. IX, p. 214.

Intracranial Tumours*Bilateral Acoustic Neurofibromas*

Bilateral acoustic neurofibromas are rarer than unilateral, and are usually part of a wide-spread neurofibromatosis (von Recklinghausen's disease). The condition may occur in children and has sometimes been hereditary. Acoustic tumours of the cerebellopontine angle may cause symptoms of bilateral pressure, and the symptoms may be so confusing that diagnosis can only be made from the presence of bilateral deafness. W. McK. Craig and E. J. Steenrod reported two cases of bilateral acoustic neurofibromas, both part of a generalized neurofibromatosis and operated upon. It was concluded that, owing to the multiplicity of the tumours and the difficulties of technique, palliative treatment was preferable.

Craig, W. McK., and Steenrod, E. J. (1938) *Arch. Otolaryng.*,
Chicago, **28**, 404

NEUROSYPHILIS

See also Vol. IX, p. 224, and Cumulative Supplement, Key Nos. 1151-1166

General Aetiology

H. H. Reese and E. R. Hodgson considered that the selective action of the *Spirochaeta pallida* on the central nervous system was due to a lack of vitamins causing a failure of protection of the tissue and its invasion by the organism. They estimated the gastric acidity and pyruvic-acid blood levels in 168 cases of neurosyphilis. The blood pyruvic-acid was normal in all cases, and 43 patients had low free-acid curves. They concluded that those cases studied did not show a vitamin deficiency. Nevertheless, they found that treatment with large doses of vitamins effected improvement even before specific treatment was begun, and subsequently they found that the 2 treatments did not antagonize each other.

Reese, H. H., and Hodgson, E. R. (1939) *Urol. cutan. Rev.*, **43**, 56.

General Paralysis of the Insane*Aetiology*

M. Glatt examined the question as to whether any relation existed between the outbreak of general paralysis and specific treatment of syphilis. Patients in whom signs of general paralysis started between 1925 and 1935 were examined. No definite difference was observed in the length of the latent period between those cases which were cured by specific treatment soon after syphilitic infection and non-specifically treated cases. The author's material did not support the opinion that the incubation was diminished by salvarsan (arsphenamine). Intensive treatment by salvarsan gave relatively the best result. The average latent period became increased. This was probably due in the first place to an increase of the latent period in treated cases. The average age of outbreak of general paralysis was also increased. The opinion that modern treatment of syphilis furthered development of general paralysis was not supported by the author's material.

Treatment

Cerebral impaludation. M. Ducoste gave the name 'cerebral impaludation' to the method of treating dementia paralytica which consists of injecting a few cubic centimetres of blood containing the malarial organism into the interior of the encephalon. He used this method in the hope of breaking down the encephalo-lymphatic barrier which prevents the penetration of therapeutic agents into the nerve centres. The injection was made into one frontal lobe, or into the 2 lobes at the same time, the malarial blood being mixed with an equal amount of tetanus antitoxin, 3 to 5 c.cm. of the mixture being used. The operation was without adverse effect although the temperature may rise for a short time 1 to 1.5° C. a few hours afterwards. In 550 cases there was only one death which the author regarded as coincidental. The injection can be repeated after a few days or a few

months. The malarial fever began most commonly on the seventh or eighth day after injection and schizonts were nearly always found in the blood in small numbers. Quinine was given to interrupt the fever. Of the patients 81 per cent were cured, 13 per cent did not respond, and 6 per cent died from intercurrent diseases several months or years after the operation.

T.A.B. vaccine.—C. E. Roachsmith and E. S. Stern reported the treatment of male general paralytics since July 6, 1928, by injections of T.A.B. vaccine containing 1,000 million dead *B. typhosum* and 750 million each of dead *B. paratyphosum* A and B per c cm. Injections were given on alternate days beginning with 0.1 c cm. and increased up to 1 c cm. More than one course was usually given, and also 2 g. of neoarsphenamine. A rigor usually occurred about half an hour after the injection, followed within one hour by fever up to 105° F. lasting about 3 hours, exceptionally the temperature reached 107° F., or continued for 24 hours or more. It was remarkable that patients who ultimately recovered were lucid during the fever, then at once relapsed, only showing lasting recovery a few weeks later. Moribund patients and those with aortic disease were unfit for this treatment, and collapse, seizures, or repeated vomiting were indications for discontinuance of the treatment. Ninety patients were thus treated, but for statistical purposes direct admissions only, who had not been given fever treatment elsewhere, were utilized. Of 75 patients 18, or 24 per cent, were discharged (to work in 11), and 46, or 61 per cent, died. These results were much the same as those obtained by other methods of fever treatment, but the T.A.B. method was less severe than malarial therapy, no case proving directly fatal from the injection of T.A.B. vaccine. It was pointed out that general paralysis had become both less frequent and less severe.

Ducoste, M. (1938) *Arch. Neurol. Psychiat.*, Chicago, **40**, 707.

Glatt, M. (1938) *Conf. neurolog.*, **1**, 257.

Roachsmith, C. E., and Stern, E. S. (1939) *J. ment. Sci.*, **85**, 558.

Spinal Neurosyphilis

Juvenile Tabes

M. Várady describes a case of juvenile tabes dorsalis, which is an unusual manifestation of congenital syphilis. The symptoms differ from those of tabes in adults in so far as pain (neuralgia, girdle pain) and trophic disturbances are absent. No improvement followed pyrotherapy and antisymphilic therapy.

S. Wendt in recording 2 cases of juvenile tabes pointed out that up to the time of writing there were only about 140 recorded cases.

Tabes Dorsalis

Treatment. P. A. O'Leary and seven co-workers found that of 5,293 tabetics, whose cerebrospinal fluid had been examined more than once, 40 per cent showed clinical evidence of neurosyphilis and a positive cerebrospinal fluid. The report is based on the records of 985 patients taken from this group. It was concluded that routine treatment reversed the reaction of the cerebrospinal fluid in many cases, and should consist of at least 8 injections of arsphenamine to a course, and twice as much of a heavy metal, such as bismuth or mercury. The use of a soluble mercurial salt daily, simultaneously with the course of arsphenamine, appeared to produce a higher incidence of improvement than a combination of the latter and a bismuth preparation. The continuous daily use of a soluble mercurial salt is not practicable and, in its place, the injection of a soluble salt of bismuth in solution was advised—2 injections a week, each containing a minimum of 35 mg. of metallic bismuth. Failing any improvement, and if the clinical manifestations indicate a comparatively early stage of the disease, intraspinal treatment in conjunction with routine treatment offers the highest percentage of clinical and serological improvement. The techniques used for intraspinal treatment were the Swift-Ellis, the Swift-Ellis-Ogilvie, or the Wile modification of the Ravaut technique. Among those patients whose cerebrospinal fluids show a curve of the dementia paralytica type, malarial therapy, if used early in the course of the disease and followed by intraspinal injection, produced satisfactory clinical and serological results. In the estimation of the value of the various remedies, it was found that intraspinal therapy was more effective in the prevention of clinical advance of the disease than the other therapeutic measures, but among patients who have signs of advanced tabes dorsalis this course was not recommended. It was suggested that, if there is not a satisfactory response to one of the supplementary types of treatment, a change to one of the other supplemental

methods may be advisable, as in a small proportion of cases in which resistance is high, satisfactory clinical and serological results follow a combination of the three auxiliary treatments

O'Leary, P. A. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 692.

Várady, M. (1938) *Arch. Kinderheilk.*, **115**, 176.

Wendt, S. (1938) *Acta paediat.*, **23**, 242

NOSE AND NASOPHARYNX DISEASES

See also Vol. IX, p. 256, Cumulative Supplement, Key No. 1168; and p. 90 of this volume.

Chronic Hyperplastic Rhinitis

Treatment

Glucose solution injections—M. Baer recommended the use of local injections of 50 to 60 per cent glucose in the treatment of chronic hyperplastic rhinitis. Radical methods of treatment often cause atrophic rhinitis, and the author's experiments have convinced him of the superiority of this method of treatment. The solution is injected submucously into the conchae, and no untoward incidents are to be expected.

Baer, M. (1939) *Msch. Otolaryng.*, **73**, 108

Folliculitis Naris Perforans

R. B. Palmer described a case of folliculitis naris perforans. The condition is rare, and consists of a chronic pustule on one or other side of the median line of the tip of the nose on the cutaneous surface. A hair is present in the centre of the lesion with its bulbous end pointing towards the skin. When this hair is removed the lesion heals, as happened in Palmer's case, although his patient also subsequently received a small dose of X-rays. The condition is said to be due to the infection of a hair follicle within the nostril, with the result that the hair becomes devitalized and separated from the papilla. The pustule closes on the inner nostril side because of debris and serum, and therefore, as it progresses, points on the skin surface. The presence of the hair in the pustule acts as a foreign body, and prevents its healing. Its removal cures the condition.

Palmer, R. B. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 429.

Fracture of Nasal Bones

Treatment

From an analysis of 100 cases of fracture of the nasal bones, J. W. Gerrie concluded that practically all are impacted, either laterally or vertically, and advocated reduction as soon as possible, regardless of swelling or laceration. A general anaesthetic was preferable to local novocain-adrenaline solutions. For reduction, two haemostats with the tips wrapped in absorbent cotton were used. One in each nostril is carried to a position underneath the nasal crest. In the vertical form of impaction it was only necessary to reduce the impaction of the fragments by lifting, and to mould them by the fingers into their proper position. Reduction of the lateral impaction type was more difficult, and it was essential that the fragments were disimpacted. With this object the haemostat in the nostril away from the side of impact should with some force raise the overriding fragment, while the haemostat in the other nostril lifts the impacted fragment outwards; then the finger and thumb externally guide the parts into their correct positions. With the same haemostats or the blade of a duck-bill forceps, valuable adjustments of the torn or dislocated septum can often be made to ensure an airway and obviate later submucous resection. A modification of the Watson-Williams internal splint was used, and, in order to minimize post-operative oedema and to give the patient an added sense of security, an external, gauze-wrapped, dental impression compound splint was placed over the dorsum of the nose, and kept in position by adhesive strapping.

Gerrie, J. W. (1938) *Canad. med. Ass. J.*, **39**, 433.

OEDEMA

See also Vol. IX, p. 268.

Infantile Oedema

Treatment

Vitamin B₁.—A. Kollmann reported on the use of vitamin B₁ in infantile oedema of alimentary origin. This therapy was based on the observations of the close connexion between avitaminosis B and marasmus. All the infants treated suffered from severe nutritional disturbances and restricted nourishment, and fluid diet invariably produced marked oedema. The use of vitamin B₁ resulted in a speedy reduction of the oedema and immediate loss of weight. The author concludes that vitamin B₁ has a marked diuretic action, as it regulates the fluid balance of the organism. He therefore advises its use in all cases of hydrolability.

Kollmann, A. (1939) *Arch. Kinderheilk.*, **117**, 64.

OEDEMA, HEREDITARY

See also Vol. IX, p. 282.

Clinical Picture

M. Cooperstock classified congenital enlargement of the extremities into (i) lymphoedema (Milroy's disease), which was qualified as lymphangiectasis, (ii) haemangiectatic hypertrophy, and (iii) von Recklinghausen's neurofibromatosis. The first form was characterized by the presence at birth of a non-pitting oedema of all or part of the limb, and might be familial. There was neither pain nor changes in the skin. Macroscopically the skin and deep fascia appeared normal, but the distance between them was increased. Microscopically the space normally occupied by the subcutaneous fat contained widely dilated lymphatic spaces and fibrous tissue. X-ray examination showed absence of thickening in tissues other than the skin. Lymphoedema might appear first at puberty, its aetiology was unknown. Congenital haemangiectatic hypertrophy of the extremities was characterized by overgrowth with increased vascularity; the veins alone or both veins and arteries might be dilated, the condition was probably due to abnormal arteriovenous anastomoses, namely direct communication between artery and vein without the intervention of capillaries. The accelerated growth of the extremity was due to the increased vascularity. Both the soft tissues and bone were affected and the enlargement occurred both in length and circumference. Ulceration and gangrene might follow. Cardiac enlargement might result from increased venous pressure. Pigmentation of the skin of the limb was common. Von Recklinghausen's neurofibromatosis might cause disturbances of growth, and morbid changes in the bones, such as irregular overgrowth and cyst-formation as shown by X-ray examination. The value of X-ray examination in the differential diagnosis of the 3 forms was emphasized.

Cooperstock, M. (1939) *Amer. J. Dis. Child.*, **57**, 309.

OESOPHAGUS DISEASES

See also Vol. IX, p. 287, and p. 43 of this volume.

Acute Oesophagitis

Due to Thrush

That thrush was not necessarily benign was shown by J. H. Ebbs, who reported 22 cases of oesophagitis in infants due to this condition. The outstanding signs and symptoms were the presence of oral thrush, refusal to take food, vomiting during or soon after feeding, severe toxæmia, in some cases the presence of blood in the vomit, and even in a few cases melaena. Broncho-pneumonia was a common terminal event. The lesions were ulceration of the epithelium and invasion of the submucosa by the mycelium of the thrush fungus. That repeated painting of the oral thrush with gentian violet could influence oesophagitis was shown by the recovery of one patient. Cases were also reported of diphtheria (2 cases: see Plate IV), tuberculosis (1 case), and Vincent's angina (1 case) of the oesophagus in infancy.

Ebbs, J. H. (1938) *Arch. Dis. Childh.*, **13**, 211.



Case 8. Oesophagus and stomach from child of 2 months with diphtheria of oesophagus and superimposed or coincidental thrush infection, showing ulceration and membrane (From *Archives of Disease in Childhood*, 1938)

PLATE IV

Peptic Ulcer of the Oesophagus*Clinical Picture*

F. Norgaard reported a case of peptic ulcer of the oesophagus in a girl, aged 3 years, which was diagnosed by X-ray examination. When 3 years old she was vomiting, emaciated, anaemic, and had scurvy. Radiologically there was narrowing, leaving only a string-like passage in the lower third of the oesophagus with dilatation above. She relapsed when 7 years old, and had haematemesis and melaena, emaciation, anaemia requiring blood transfusion, and severe pain for which morphine was necessary. Atropine had some beneficial effect on the vomiting which was frequent and copious. Treatment consisted in the administration of sodium bicarbonate, which relieved the pain, and the passage of a duodenal sound which was left in position for long periods. The literature of the subject was reviewed. Peptic ulceration of the oesophagus might occur at any age from birth to extreme old age. The symptoms were pain behind the sternum or in the back, started by swallowing or delayed for 30 minutes or an hour; or there might be purely gastric symptoms including haematemesis. Radiological examination was sometimes negative; the commonest appearance was spasm, very rarely spasm and a contrast-filled ulcer niche have been seen. Broad folds of mucosa, indicating oesophagitis, have sometimes been described. Unless the condition was treated, the prognosis was bad, as perforation was prone to occur into the great vessels or the pleural cavity. In a few cases islands of heterotopic gastric glands secreting acid had been found in the wall of the oesophagus.

Norgaard, F. (1938) *Acta Radiol., Stockh.*, **19**, 458.

OVARY DISEASES

See also Vol. IX, p. 318.

General Differential Diagnosis

P. Bernstein found that the incidence of ovarian lesions in young, normally menstruating, unmarried women, complaining of lower abdominal pain, was high. Many of these cases were diagnosed as appendicitis, and some were submitted to operation. In 45 patients diagnosed as chronic appendicitis no pathological change was found in the appendix, and in 58 patients diagnosed as acute appendicitis only 4 appendicular lesions, sufficient to justify operation, were found. Ovarian disease accounted for 96 per cent of abnormal operative findings, though only 14 per cent of the conditions found justified surgical removal.

Bernstein, P. (1938) *Arch. Surg., Chicago*, **37**, 1004.

Tumours*Dysgerminoma (Seminoma Ovarii, Oophoroma Folliculare)*

M. B. Dockerty (1939, b) reported 9 cases of this solid ovarian tumour which histologically resembles a seminoma of the testis, but clinically is much less malignant. It is often associated with gonadal hypoplasia and sometimes with pseudo-hermaphroditism. The tumour does not produce any hormone, menstrual or sex disturbances, and has been regarded as occupying a neutral position between the masculinizing arrhenoblastomas and the feminizing granulosa-celled tumours. They usually occur before the age of 20 years. Among 400 solid ovarian tumours there were 9 dysgerminomas at the Mayo Clinic. The percentage of malignant cases is estimated as 45 as compared with 25 per cent for arrhenoblastomas, and 5 per cent among granulosa-celled tumours. Dysgerminomas, described under various names, such as embryonal carcinoma, carcinosarcomatodes and giant-cell sarcoma, have probably been reported in 200 cases.

G. E. Seegar analysed 79 cases of Brenner tumour; these are rare, constituting 3 per cent of all malignant ovarian tumours (Klaften). The patients are usually under the age of 30, and in some cases there is malformation of the genitalia. The right ovary was involved in 48 per cent, and in 26 per cent the growth was bilateral. The tumour does not contain the gonadotrophic hormone. Meyer regarded the tumours as relatively benign, whereas Klaften regarded them as highly malignant; from the histological appearance Seegar could not distinguish the innocent from the malignant forms. Treatment should be excision, but if they are inoperable irradiation should be employed.

Granulosa-Celled Tumour (Feminizing Tumour)

M. B. Dockerty (1939, a), in an abstract of a paper to be published in full, analysed 30 examples of the feminizing granulosa-celled tumours among about 400 solid ovarian tumours at the Mayo Clinic between the years 1910 and 1937. One of them, probably the largest on record, weighed 15.9 kg (35 lb.) More than 300 cases had now been reported, in 90 per cent they were non-malignant, unilateral, and solid; 60 per cent occurred after the age of the menopause, and 5 to 10 per cent before adolescence. From the large amount of oestrogen secreted by the tumours they caused recurrent periodic bleeding after the age of the menopause, precocious menstruation before puberty, and between puberty and the menopause either amenorrhoea, or amenorrhoea followed by profuse and continuous menses.

Arrhenoblastoma (Masculinizing Ovarian Tumour)

M. B. Dockerty and V. S. Counseller reported 4 more cases of the masculinizing ovarian tumour arrhenoblastoma in a series of 400 solid ovarian tumours seen at the Mayo Clinic from 1910 to 1937. The number of recorded cases now reaches about 35. Norris collected 38 and accepted 29 in 1938. There are two views about the origin of the tumours: (a) from embryonic remains of seminiferous tubules in the hilum of the ovary, (b) from a one-sided teratoma. In these usually solid tumours the epithelial cells are arranged as a tubular adenoma, as a diffuse sarcoma, or as a cylindroid pattern. Most authors agree that three-quarters of the cases are relatively benign, the tumours are extremely radio-sensitive (Norris). The clinical change is towards a male habitus and secondary male characters only, hypertension and disturbance of sugar tolerance are more likely to occur in Cushing's syndrome and the adreno-genital syndrome. Enlargement of the clitoris may be excessive. The breasts diminish in size or in the young show arrested growth. The tumour has never been present in both ovaries (Counseller).

L. Novak described the features of 11 cases of masculinizing tumours of the ovary including 6 new cases. He described 2 kinds of tumours which may produce this condition, the arrhenoblastomas and the rare ovarian tumours composed of adrenal tissue. The patients showed evidence of defeminization and masculinization in growth of hair of the male distribution, deepening of the voice, enlargement of the clitoris, flattening of the breasts, amenorrhoea, and a general angulation of the body contours. Removal of the tumours was followed by a return towards normality, but this was not always complete.

Masculinovoblastoma (Masculinizing Ovarian Tumour)

Under the title masculinovoblastoma, a primary masculinizing tumour of the ovary (so-called large-celled variety—hypernephroid—luteoma) A. Rottino and J. F. McGrath described 2 cases and collected 7 other cases regarded as similar in nature. The tumour was distinct from the ovarian arrhenoblastoma, the masculinizing tumour, and the alternative titles referred to the views: (i) that the tumour arose from adrenal cortical cells included in the ovary, a tumour homologous to Grawitz's hypernephroma of the kidney, and (ii) that it was a tumour of lutein cells of the ovarian follicle. The 2 cases described arose in the ovary, one being benign, and, like the collected cases, unilateral, the other case was malignant, and both ovaries were affected. In both cases removal of the ovaries was followed by disappearance or some diminution (the malignant case) of the masculine character. The arguments in favour of the adrenal and of a lutein origin were frankly set out and, while the difficulty in coming to a conclusion was fully recognized, the origin from an adrenal 'rest' in the ovary seemed to be the more probable. Clinical evidence suggested an interplay of the tumour with the pituitary.

Ganglioneuroma

A ganglioneuroma of the ovary containing adult ganglion cells in a negro girl, aged 4 years, was recorded by H. C. Schmeisser and W. A. D. Anderson who regarded it as unique, having examined McFarlane's collection of 93 cases of retroperitoneal ganglioneuromas. As it may have arisen from the sympathetic, it may be regarded as of extrinsic origin.

Dockerty, M. B. (1939, a) *Proc. Mayo Clin.*, **14**, 298

— (1939, b) *ibid.*, **14**, 545

— and Counseller, V. S. (1939) *ibid.*, **14**, 369.

- Klaften, E. (1933) *Zbl. Gynak.*, **57**, 36.
 McFarlane, J. (1931) *Arch. Path.*, **11**, 2005.
 Norris, E. H. (1938) *Amer. J. Cancer*, **32**, 1.
 Novak, E. (1938) *Amer. J. Obstet Gynaec.*, **36**, 840
 Rottino, A., and McGrath, J. F. (1939) *Arch. intern. Med.*, **63**, 686
 Schmeisser, H. C., and Anderson, W. A. D. (1938) *J. Amer. med. Ass.*,
111, 2005.
 Seegar, G. E. (1938) *Arch. Surg., Chicago*, **37**, 697

OXYCEPHALY

See also Vol. IX, p 346, and Cumulative Supplement, Key No 1198.

Treatment

Surgical

In oxycephaly many operations to enlarge the cranial cavity have been attempted. Unilateral or bilateral subtemporal decompression, resection of the optic canals to prevent pressure on the optic nerves, and circular resection of the skull are examples. J. F. J. King did not believe that any of these operations would permit symmetrical expansion and growth of the skull and brain. He devised an operation, performed in 2 stages, consisting of dividing the bones of the cranial vault so that they formed a mosaic and the brain could expand beneath them. The operation could be done in one stage, especially in infants, through an 'autopsy incision'. He described the results in a patient aged 8 who was so treated. The exophthalmos was reduced, the vision improved, and the mentality and personality became brighter.

King, J. F. J. (1938) *Arch. Neurol. Psychiat.*, **40**, 1205

OZAENA

See also Vol. IX, p 354, and p 90 of this volume

Treatment

Progesterone

J. K. Willson-Pepper and H. Royle described a case in which the patient had suffered from menorrhagia for 2 years and severe spasmodic rhinorrhoea for 18 months. No evidence of nasal infection had been found after examination by an ear, nose, and throat surgeon or after radiography. In an endeavour to treat the menorrhagia 5 international units of gestone were given intramuscularly every day for the 3 days preceding the onset of the menstrual period. Gestone is progesterone in arachis oil. After the first injection, and before the menstruation commenced, the patient was assured that the improvement in her nasal condition could not have been due to the hormone which was given for her menorrhagia. One week after the end of menstruation, the patient began a course of 5 injections of gestone, 2 international units being administered intramuscularly every second day. This postponed menstruation until the full 28 days had elapsed. No nasal congestion occurred for 5 weeks after the first injection. Eleven days after the last, the patient had a transient attack of rhinorrhoea of 30 minutes' duration. For the ensuing 2 months progesterone was injected twice weekly for the second fortnight of the menstrual cycle, and during that period only 4 attacks of rhinorrhoea, much modified in severity, took place. Since this therapy ceased the patient had had but one attack in a month.

The authors, while not desiring to be too enthusiastic about data obtained from one case, think that this therapy, if widely extended, may produce valuable results in cases of ozaena.

Surgical

J. P. Kasnetz treated 6 cases of primary, or true ozaena, in which all physical and laboratory examinations had failed to reveal any cause, by implanting an ivory plate on to the septum of the nose. Only the first case was a failure, the ivory sloughing off. In the other 5 the dreaded foetid odour was removed, and the general and social condition of the patients improved considerably. The mucosa of the nose

became free from crusts, and moist, and pink. The rationale of the method is difficult to determine, but it may be that the chambers of the nose, which are always widened in ozaena, are narrowed by the introduction of the block. Contra-indications for the use of this method are a perforated septum, an excessively thin septum, too large a nasal chamber because the size and weight of block necessary to narrow it sufficiently would be too heavy to remain in place, some constitutional conditions, and suppurative sinusitis or pansinusitis.

Kasnetz, J. P. (1939) *Arch. Otolaryng.*, Chicago, **29**, 699

Willson-Pepper, J. K., and Royle, H. (1939) *Brit. med. J.*, **1**, 974.

PAIN

See also Vol. IX, p. 359, and p. 19 of this volume

Anatomical Basis

Samson Wright stated that the sensation of pain is specific, and not a mere intensification of other sensations. He divided somatic pains into 3 kinds, skin, muscle, and periosteal or tendon pains. The generalized pain produced on pressing the tender spots in fibrositis is abolished by local anaesthesia, and is therefore referred. Muscle metabolism is a more complicated process than was formerly thought, involving not only the conversion of glycogen into lactic acid, but also the breakdown and resynthesis of adenylyl pyrophosphate, and creatinine phosphate, and the conversion of lactic acid to lactate, glycogen, carbon dioxide, and water. Acetylcholine, histamine, and adenosine also play some part. During exercise the fluid content of muscle increases by about 20 per cent. The amount of exudate pouring from the blood into the tissue spaces is enormously increased and may amount to 2 c.c. per 100 grams of tissue per minute. The main channel for draining away the excess fluid is the lymphatics.

The physiological effects of massage are obscure. The effect of superficial stroking is psychological, that of deep stroking is an accentuation of this, and that of kneading is to increase the blood supply to the part but not nearly to the extent that heat does. Massage produces no measurable metabolic changes in muscle. Local heat produces marked skin changes but, owing to the insulating effect of the fat, its effect on muscle is limited. Reactive hyperaemia is vasodilatation following temporary venous obstruction in a limb. These changes are probably due to accumulated dilator metabolites. The clinical value of reactive hyperaemia has not yet been fully explored. Pyrexial treatment of rheumatic conditions is of increasing importance. In activity or hyperpyrexia heat lost by evaporation may account for 80 per cent. of the whole as against 14 per cent. at rest. In all forms of pyrexia the basal metabolic rate rises by 7 per cent. for each 1° F. rise in body temperature. The treatment also places an increased strain on the heart and is not to be embarked upon lightly.

Wright, S. (1939) *Proc. R. Soc. Med.*, **32**, 651.

Abolition of Pain

L. Hollander found that the injection of a local anaesthetic in oil into areas of hyperalgesia and hyperaesthesia in the skin relieved the pain arising from deeper structures, whether visceral or skeletal. The solution used was 3 per cent. ethyl aminobenzoate (benzocaine), 5 per cent. benzyl alcohol, and 1 per cent. phenol in expressed oil of almond. It produced prolonged anaesthesia of the skin. The treatment was successful in cases of herpes zoster, femoral neuralgia, lumbar myositis and, in one case, for the pain arising from inoperable carcinoma of the stomach.

Hollander, E. (1938) *Arch. Neurol. Psychiat.*, Chicago, **40**, 743.

PALATE, CLEFT, AND HARE-LIP

See also Vol. IX, p. 373.

Treatment

Dental Plate facilitating Feeding

J. H. Sillman has devised a dental plate by which an infant with a cleft palate can be fed from a bottle as quickly and easily as a normal baby. This plate is inserted

before each feed. An impression is taken from the palate and a plate approximately $\frac{1}{16}$ inch thick made, of soft vulcanite where it comes in contact with the palate and of hard vulcanite on the other side. The plate should rest on the oral mucosa only, and not come in contact with the nasal mucosa. To ensure the best results, the nipple should have 3 holes large enough to release the milk when the baby touches it with his tongue, i. e. approximately the size of a 23-gauge wire. The milk must be expressed mechanically, and not by suction, as the hard palate only is covered by the plate, moreover the infant cannot cup the nipple if a hare-lip is present. The same nurses should be assigned for the feeding throughout the time the baby is in hospital. Sillman recorded 5 cases, in 4 of which the plate was successful; the infants gained weight and in no case was there any irritation of the mucosa. Stress was laid on the importance of making the plate as soon after birth as possible.

Sillman, J. H. (1938) *Amer. J. Dis. Child.*, **56**, 1055.

PANCREAS, DISEASES

See also Vol. IX, p. 386

Acute Necrosis of the Pancreas

In Japan

Nobuo Mizuto, of the Imperial University of Kyoto, pointed out the increasing recognition of acute pancreatic necrosis in Japan; in the period 1901-1905, 3 cases were reported, whereas 134 cases were reported in 1931 to 1935. Analysis of 166 cases operated upon at increasing intervals after the onset of symptoms showed that acute pancreatic oedema was the first stage of necrosis, oedema was found in 38 cases, necrosis in 96, abscess in 20, 'induration' in 8, and cyst in 4. Acute necrosis was produced in rabbits by injection of 0.8 to 1.2 c.c. of olive oil or a 10 per cent solution of pancreatin into the pancreatic duct, haemorrhage being less frequent after the injection of olive oil. *Ascaris lumbricoides* played an important part in the production of pancreatic necrosis, and in some cases *Ankylostoma duodenale* and hepatic distomiasis were present. Excessive eating, especially of fat, appeared to favour the onset. A palpable swelling in the epigastrium (Krote's sign) was important but took some time to occur, muscular rigidity was slight. Incomplete ileus was almost constant, glycosuria occurred in a third of the cases, and slight albuminuria was very frequent. Jaundice was rare.

Hiroshi Tsuji also described acute necrosis of the pancreas as seen in Japan on the basis of 68 cases. There were some differences with regard to this disease in Japan as compared with Europe and America. In the 2 continents it occurred more often in women with gall-stones, the incidence was quite different in Japan. 20 of the 68 patients were females and gall-stones were found in one only. Alcoholism played an important aetiological part, being present in exactly half the 68 cases. On the other hand, as in Europe and America, the patients were nearly all obese, and the most frequent age was 40 to 60. The onset was sudden with extremely severe pain in the epigastrium which spread towards the left scapular region, vomiting followed and became frequent, even 20 to 30 times per hour, but was never faecal. Cyanosis of the face, especially the lips, and fingers and toes, occurred in a greater or less degree in all cases and was without any relation to the severity of the other symptoms. Abdominal puncture had been employed in doubtful cases in an area dull on percussion in the left hypochondrium, and arrangements for immediate laparotomy should be made. Of 50 patients operated upon, 41 recovered, and in the 18 not operated upon, 8 died. Operation should not be performed during the period of shock, when vomiting ceases within 12 hours of the onset, or when cyanosis of the face rapidly passes off.

Associated Arrhythmia

E. L. Dittler and T. H. McGavack reported acute pancreatic necrosis followed by impure auricular flutter and fibrillation, in which necropsy did not show any organic change to account for the arrhythmia. An obese bar-tender, aged 53 years, had an acute attack of abdominal pain 6 weeks before his death. There had been 3 previous milder bouts. After admission to hospital the condition was diagnosed as coronary thrombosis; after the necropsy it was clear that the abdominal lesions—necrosis of the pancreas perforating into the duodenum and colon, and generalized

sero-fibrinous peritonitis accounted for the symptoms, the cardiac changes being ascribed to reflexes from the abdomen. Reference was made to only one similar case, that of J. Drummond, of auricular fibrillation set up by acute pancreatitis.

Dittler, I. L., and McGavack, T. H. (1938) *Amer. Heart J.*, **16**, 354.

Drummond, J. (1934) *S. Afr. med. J.*, **8**, 520.

Mizuto, Nobuo (1938) *Jap. J. Gastroent.*, **10**, 106.

Tsujii, Hiroshi (1938) *Jap. J. Gastroent.*, **10**, 123.

Calculi

Diagnosis

C. L. Gillies considers that pancreatic lithiasis may be divided into 4 groups, multiple calculi, a single calculus, multiple faceted calculi, and large fragmented calculi, the first group being the most common. The stones consist mainly of calcium carbonate. Clinical findings are in no way characteristic, and X-ray examination offers the best means of diagnosis. In the majority of cases pancreatic stones lie below a horizontal plane passing through the upper margin of the first lumbar vertebra and above a horizontal plane passing through the lower margin of the body of the third lumbar vertebra. The size of the calculi varies from the very minute, which are comparable with grains of sand, to large stones the diameter of which is as much as 5 cm. It is suggested that, in establishing the relationship of suspected shadows, the gall-bladder, duodenum, and kidneys should be identified. The passing of a duodenal tube before the taking of X-ray plates is preferable to the use of barium, as the presence of the latter in the stomach may obscure any stones which may be present.

Gillies, C. L. (1939) *Amer. J. Roentgenol.*, **41**, 42.

Congenital Cystic Disease

G. L. McWhorter recorded a somewhat complicated case of a woman, 63 years old at the time of her death, with uraemia and diabetes mellitus, in earlier life she had suffered from pain shown at a hepatico-duodenostomy and removal of the gall-bladder 14 years before her death to be associated with a large cystic dilatation of the common bile-duct. The necropsy showed that the condition was congenital cystic disease of both the biliary tract and of the two pancreatic ducts—a distinct congenital cystic entity—which must not be confused with polycystic disease of the liver usually combined with a similar change in the kidneys. It was due to malformation of the 2 anlagen which form the liver and pancreas respectively.

McWhorter, G. L. (1939) *Arch. Surg.*, **38**, 397.

Tumours

Adenoma

Clinical picture and treatment. H. Krauss operated successfully upon 2 cases of adenoma of the insular tissue of the pancreas. The main symptom of the condition is hypoglycaemia due to excessive formation of insulin. The clinical picture consists of a feeling of hunger, tiredness, and coma. The coma occurs mostly in the morning before breakfast. Injection of glucose produces immediate improvement. Absence of other symptoms distinguishes adenoma of the pancreas from Addison's disease and diseases of the pituitary. The only possible treatment for adenoma of the insular tissue is operation. This is difficult as in most cases there are several small tumours deeply embedded in the pancreatic tissue. When the tumour was removed there was a sudden improvement in the condition, and hypoglycaemic coma did not again occur.

Adenocarcinoma

Morbid anatomy and clinical picture. F. W. Grauer analysed 34 cases of primary carcinoma of the pancreas examined after death and occurring over a period of 20 years. Of these 26 were in males and 8 in females, and the fifth to the seventh decade included most of the cases. In 15 cases the head of the pancreas was the only part of the gland involved, in 11 instances the whole of the pancreas was studded with carcinomatous nodules. The carcinoma started in the ducts in 25 cases, in the acini in 7, and in the islands of Langerhans in 2 cases. The duct carcinomas were very fibrotic; the acinar tumours grew in solid masses of cells which varied in size,

some being small round cells, others elongated spindle cells. In 3 instances there were not any metastases; the regional lymphatic glands were infected in 28 cases, the liver in 25, the lungs in 16, and the skeleton in 7 cases. The earliest symptoms were due to the primary tumour in 28 and to metastases in 6 cases, these latter symptoms being pains in the limbs, e.g. sciatica. Jaundice occurred in 20 cases, being early in 6 cases, late in 9, and midway in the course of the disease in 5. The gall-bladder was palpable in 7 cases only. Ascites occurred in 6 cases. The duration varied, in 2 cases the disease lasted 7 and 5 years, in 2 cases 3 years, in 2 more than 2 years, and in 28 cases less than a year.

E. H. Norris *et al.* record a case of atrophy of the pancreas with extreme fatty metamorphosis of the liver with steatorrhoea, due to a small scirrhous adenocarcinoma in the head of the pancreas. The tumour did not involve the ampulla of Vater, and there was not any biliary obstruction or jaundice; the pancreatic ducts, however, were completely blocked, and the pancreas was so atrophied that it was recognized more by its position than by its naked-eye appearances. In the case reported by Norris and his co-authors the symptoms were those of sprue, and the pancreas, except the islands of Langerhans which were normal, was extremely atrophied.

Treatment —C. F. W. Illingworth described a case of primary adenocarcinoma of the head of the pancreas in a man aged 59 with obstructive jaundice and distension of the gall-bladder. Though the operation, from the relations of the head of the pancreas to the portal vein, the common bile-duct, and the duodenum, was beset with difficulties, it was pointed out that carcinoma of the head of the pancreas presented two features of a favourable character: (i) it was at first a local lesion, slow in growth and in metastasis, and (ii) it could be diagnosed in an early stage. In the past, surgical treatment had been palliative, namely relief of the jaundice by drainage of the gall-bladder into the gastro-intestinal tract. In this case the radical removal was carried out in 2 stages. The first operation consisted of cholecyst-gastrostomy and gastro-jejunostomy, 8 weeks later the head and neck of the pancreas, the greater part of the duodenum, and the affected portions of the bile and pancreatic ducts were removed. Both operations were well borne, and the patient, greatly improved, left hospital. Unfortunately 5 weeks later sudden abdominal pain, vomiting, and constipation supervened. This was due to leakage from the cut end of the common bile-duct which caused biliary peritonitis and death.

Grauer, F. W. (1939) *Arch. intern. Med.*, **63**, 884.

Illingworth, C. F. W. (1939) *Lond. med. J.*, N.S. **46**, 331.

Krauss, H. (1939) *Deutsch. Z. Chir.*, **251**, 512.

Norris, E. H., Beard, A. H., and Gerber, W. S. (1938) *Arch. Path.*, **26**, 1234.

PANNICULITIS

B. Shaffer describes fully a case of liquefying nodular panniculitis, which is differentiated from relapsing febrile non-suppurative nodular panniculitis by several outstanding features. The most obvious of these is the breaking down of the lesions, which occurred in the reported case, with associated liquefaction, subsequent rupture, and discharge. Deep-seated, painful, and tender nodules appear in the subcutaneous fatty tissues, changing within 10 days into cystic masses containing one to 4 ounces of oily yellowish-brown fluid. Later, a deep cuplike depression in the subcutaneous fat is associated with a thin scar at the site of the healed lesion. In the non-suppurative type (Weber-Christian syndrome) the lesions undergo spontaneous absorption and involution. Other differentiating factors are the tenderness associated with the lesions and discoloration of the skin. In the case described the areas affected were the buttocks, thighs, and extremities. The temperature ranged from 100 to 103° F. but, even after it became normal, small numbers of lesions continued to appear. The cause of the condition remained undetermined. Treatment consisted of injection of neoarsphenamine and of gold sodium thiosulphate. The effects were satisfactory, but proved only temporary. At the time of the report the patient had been free of recurrences for 6 weeks.

Shaffer, B. (1938) *Arch. Derm. Syph.*, N.Y., **38**, 535.

PAPILLOEDEMA

See also Vol. IX, p. 396.

Morbid Anatomy

B. Samuels examined after death 50 globes from 47 individuals in whom papillo-oedema had been diagnosed during life. Clinically each papilla presented a typical swelling (choked disc) as the outstanding feature. In 31 cases numerous causes were incriminated, such as cerebral tumour, meningitis, nephritis, exophthalmos, anaemia, angioma of the choroid, and hypotony. There were only 14 cases of brain tumour, which is remarkable in view of the clinical frequency of brain tumour as the cause of papilloedema; this was explained on the ground that patients with cerebral tumours do not usually die while the swelling is at its maximum.

By means of photographs an accurate record can be kept of the varying phenomena of papilloedema. In a papilla clinically showing moderate swelling there would probably be microscopical evidence of compression of the neuro-epithelial layers of the retina. In the atrophic stage little or no change in the pigmentation at the margins of the disc could be expected, and such a nerve-head could not be differentiated clinically or pathologically from one of primary atrophy. The papilla in which the swelling is clinically high on the nasal side and relatively low on the temporal side would be apt to show displacement of the neuro-epithelium on the nasal, and compression on the temporal, side. Considerable swelling of the papilla with steep margins would correspond clinically with those cases seen pathologically with a large circumpapillary space filled with the characteristic tissue. Dilatation of the retinal vessels indicated constriction in the capillaries caused by folds in the deeper layers. When the enlarged blind spot could not be accounted for by the breadth of the papilla, the existence of a slit-like detachment of the retina should be suspected. Over such a detachment the retina was usually but little folded. In very considerable oedema much of what was seen was not optic nerve but a broad zone of cystic retina and circumpapillary tissue.

When complete atrophy had supervened no vestige of circumpapillary tissue would be visible ophthalmoscopically because it disappeared with the nerve fibres. A disturbance of pigmentation should be looked for clinically on the nasal side, either at the immediate margin of the disc or at a considerable distance away. These were the only permanent tracks left by the circumpapillary tissue. Routine examination of the macular region for evidence of cystic degeneration was recommended in all cases of papilloedema.

Samuels, B. (1938) *Amer. J. Ophthalm.*, **21**, 1242

PARALYSIS AGITANS

See also Vol. IX, p. 408.

Treatment*Bulgarian Belladonna Root*

N. S. Alcock and E. A. Carmichael investigated on behalf of the Medical Research Council the claims made for Bulgarian belladonna in the treatment of paralysis agitans. The comparative effects of 4 groups of drugs were investigated: (i) decoction of Bulgarian belladonna root, (ii) English belladonna used as (a) tincture B.P., and (b) decoction; (iii) stramonium (a) the B.P. 1932 tincture, (b) dried extract of stramonium, U.S.P., (c) a decoction of Bulgarian root, and (iv) trasantin. The Bulgarian decoction was first given in a dosage of 2 c.cm. last thing at night. It was increased slowly to a maximum of 20 to 26 c.cm. twice daily. Dryness of the mouth became troublesome when the dose reached 8 to 10 c.cm. twice daily, and, at slightly over this level, paralysis of accommodation supervened, coming on at first for an hour or two after the dose, and later becoming permanent so long as the administration of the drug was continued. A clear week or more without medication was arranged between giving stramonium and Bulgarian belladonna to ensure that the patients had returned to their original untreated state. To obtain an objective comparison between the effect of the various treatments, graphic records were taken by a modified ergograph, flexion and extension at the elbow being recorded on a smoked drum. In all cases large doses of Bulgarian decoction were of undoubted

benefit, but results obtained with English belladonna were equally good, and with stramonium perhaps even slightly better.

W. Voller treated 173 patients with encephalitis epidemica and paralysis agitans with an extract from the root of *Atropa Belladonna* on lines modified from those of Ivan Rajew and Antolini-I rugoni. Rajew advocated a 5 per cent infusion of the root in white wine, which proved to be rather toxic. Voller employed an infusion of the root in water with an alkaloid content of 0.2 per thousand; the average dose was 50 to 70 c.cm. in 24 hours, given 3 hours after a meal to avoid any digestive disturbance. It was very important to avoid meat, spirits, and tobacco. Massage, exercise, and psychotherapy were recommended. The improvement was remarkable, even in completely disabled patients, paralysis and salivation and hyperkinetic manifestations disappeared. The treatment is contra-indicated in cardiac and renal disease, glaucoma, eczema, diabetes mellitus, and diseases of the blood.

Alcock, N. S., and Carmichael, E. A. (1938) *Quart. J. Med.*, N.S. 7, 565

Voller, W. (1938) *Munch. med. Wschr.*, 85, 1703.

PARATHYROID GLAND DISEASES

See also Vol. IX, p. 424

Hypoparathyroidism

Treatment

I. A. Anderson and A. Lyall in a paper on the treatment of chronic hypoparathyroidism recorded the results of metabolic investigation of 3 cases following thyroidectomy and summarized the present state of opinion on the treatment of this condition. The treatment of parathyroid deficiency, whether post-operative or of the so-called idiopathic form is divisible into (i) the acute stage, especially with spasms of tetany, which usually yields readily to the intravenous injection of calcium salts, with or without intramuscular injection of parathyroid extract, and (ii) chronic hypoparathyroidism in which the above treatment is not suitable. Their metabolic observations on the calcium and phosphorus in the blood were carried out on the 3 patients first when on a high calcium diet with a relatively high phosphorus intake, and then on a low phosphorus diet in which the calcium intake was maintained at the previous high level by the necessary addition of calcium lactate. The results showed that the serum calcium can be kept at the normal level by the administration of a diet low in phosphorus and large doses of calcium lactate. No additional treatment in the form of vitamin D or acid was given, except in one of the patients with chronic nephritis who was given enough hydrochloric acid to counteract the alkalizing effect of the calcium lactate.

Dihydrotachysterol.—C. M. MacBryde treated 6 women suffering from chronic hypoparathyroidism following thyroidectomy and one case of idiopathic tetany with dihydrotachysterol. The length of history in these cases had varied from 3½ to 17 years. Previous therapy had been quite useless. The drug is a derivative of irradiated ergosterol and is employed in an oily solvent containing 5 mg. per c.cm. They found that small doses by mouth would keep the blood-calcium level normal and relieve the tetany but that larger doses were needed if no additional calcium was given. In acute cases it is best to give intravenous injections of calcium and intramuscular injections of parathyroid extract. In chronic cases parathyroid extract loses its effect but dihydrotachysterol does not and is excellent in the treatment of such cases. Normal serum calcium values were subsequently maintained with dihydrotachysterol 0.3 to 1 c.cm. daily supplemented by 4 to 10 g. a day of calcium lactate or calcium gluconate.

F. Albright reviewed the modern simplified method of treatment of hypoparathyroidism and pointed out that this disease does not require specialist laboratory facilities. Dihydrotachysterol, a photochemical derivative of ergosterol, raises the blood-calcium level, which is all that is needed in this condition. The blood-calcium determination is of only secondary importance. The Sulkowitch test for differentiating urines containing no calcium, a small amount of calcium, and a large amount of calcium can be carried out by the patient. The reagent is a buffered solution of oxalate radicals; when equal amounts are added to the urine a fine white cloud precipitates if the calcium content is satisfactory. There are variations between the

blood-calcium level and the urine calcium, but for practical purposes it is enough to carry out the above test, and keep the patient on a high-calcium diet.

Calcium lactate.—That calcium lactate dissolved in water and given orally raises the serum calcium has been shown by experiment. It is therefore unnecessary to give intravenous injections of calcium or parathyroid extract for parathyroid deficiency. Watery solutions of calcium carbonate, glycerophosphate, and chloride are less effective than calcium lactate, and calcium bicarbonate, given by this method, produces no elevation in the serum calcium. S. J. Wilson describes a case of tetany following thyroidectomy which was treated with intravenous injections of calcium gluconate. These were given repeatedly and finally calcium lactate 30 gr. dissolved in water was given orally. The symptoms ceased and the serum calcium rose. Calcium lactate in tablet form and in milk was not effective in this case.

Bone graft implanted subcutaneously. W. M. Woskressenski of Leningrad discusses the existing methods of treatment of tetany in adults and refers to the method of Oppel, which consists in implanting a bone graft under the skin; this increases the calcium level in the blood and stimulates the parathyroid glands. A piece of bone, measuring about $2 \times 4 \times 0.5$ cm. and polished, is boiled for 24 hours in a 2 per cent solution of sodium carbonate. Shortly before implantation the bone is boiled again for 2 hours in physiological solution of sodium chloride. The piece of bone is inserted into a pocket in the pectoral muscle under the fatty tissue of the breast. The treatment is successful only in cases of real tetany confirmed by a low calcium level in the blood, and by the signs of Wernon, Trouseau, and Bechtereff. In very severe cases of tetany the implantation is not curative but ameliorates the condition. In 11 cases of real tetany the author obtained 9 complete cures and one improvement, in one case other treatment had to be used in addition to the implantation.

Albright, F. (1939) *J. Amer. med. Ass.*, **112**, 2592.

Anderson, I. A., and Iyall, A. (1939) *Quart. J. Med.*, N S **8**, 209.

MacBryde, C. M. (1938) *J. Amer. med. Ass.*, **111**, 304.

Wilson, S. J. (1938) *Arch. Surg., Chicago*, **37**, 490.

Woskressenski, W. M. (1938) *Rev. Chu., Paris*, **57**, 633.

Hyperparathyroidism

Diagnosis

Hamilton and Highman's test—D. R. Gilligan *et al.* undertook tests, using the Hamilton and Highman method, to detect abnormally large amounts of parathyroid hormone in patients with chronic nephritis, toxic goitre, and Paget's disease of bone. A rise of 0.3 mM. per litre in the serum calcium of a test rabbit, either at a 3-hour or 5-hour period, was held to be a positive reaction. In 13 out of 14 cases of chronic renal insufficiency, parathyroid hyperfunction was not indicated. The test should clarify the relation between anatomical findings and function, but the authors feel that the results obtained with the Hamilton and Highman test are not reproducible in the hands of other investigators, and that the significance of the test is, at present, questionable.

Morbid Anatomy

Renal changes—W. A. D. Anderson reported 3 cases of parathyroid tumours associated with kidney damage. In the first patient, a woman, aged 47, there had for more than 12 years been mild hyperparathyroidism and bilateral renal colic and the passage of small calculi. Six years later nephrectomy and removal of a calculus were carried out on the right side. Six months after removal of a parathyroid tumour, which was followed by improvement, she died at home, the cause of death being doubtful, but the kidneys were examined and showed massive interstitial calcification and other changes. The second case showed irregular thickening, calcification, and degeneration of the basement membranes of the convoluted tubules. The epithelium of the tubules was damaged and calcified masses partly filled the collecting and convoluted tubules; interstitial fibrosis and calcification, as in case 1, were also present. The third case, a male renal dwarf, aged 19 years, had had symptoms from birth. Most of the glomeruli appeared normal. The outstanding change was in the interstitial tissues adjacent to the tubules and the glomeruli, calcium deposits often formed a sleeve around the tubules. The interstitial connective-tissue was greatly thickened in the cortex. The tubular basement membrane was thickened and calcified in some areas. The lining epithelium of the tubules was undamaged. In some places the heavily calcified interstitial tissue between dilated tubules had broken down to

form spaces containing masses of calcified material. This appeared to be the early stage in the formation of small calculi in the substance of the kidney. There were only slight vascular changes. As this patient was a renal dwarf, it would seem probable that the parathyroid hyperplasia was secondary to renal deficiency. Fifty kidneys containing calcium deposits and not associated with parathyroid tumours were examined, but in no case was there a condition similar to that in the 3 cases; it was therefore concluded that the changes in the kidneys of the 3 cases were those due to chronic hyperparathyroidism. To recapitulate, the characteristic renal changes due to chronic hyperparathyroidism were interstitial fibrosis, calcification and infiltration by lymphocytes and plasma cells, cystic tubular dilatation, thickening and sometimes calcification of the tubular basement membrane, and relative absence of active glomerulitis or involvement of the tubular epithelium. The interstitial calcium deposition was mainly peritubular and subsequent to damage of the kidney substance.

Anderson, W. A. D. (1939) *Endocrinology*, **24**, 372.

Gilligan, D. R., Volk, M. C., and Gargill, S. L. (1938) *J. clin. Invest.*, **17**, 641.

PAROTID GLAND DISEASES

See also Vol. IX, p. 449.

Diagnosis

Sialography

J. V. Blady and A. F. Hocker present a series of 38 cases of non-neoplastic affections of the parotid gland studied by sialography. The conditions include acute and chronic parotitis, salivary fistulae, calculi and stricture of Stensen's duct. For an injection of lipiodol (iodized oil) the patient should be in the sitting position. The mucous membrane surrounding the duct orifice is anaesthetized by 10 per cent cocaine hydrochloride. The location of the duct orifice is in the papilla of the buccal mucous membrane adjacent to the second upper molar tooth. The duct is dilated with a lacrimal dilator or tempered probe. The injection should be carried out slowly, the minimum amount of lipiodol exceeding 1 c.c., and the maximum less than 1.75 c.c. To prevent the escape of the lipiodol, the patient compresses the orifice of the duct by squeezing the cheek between the thumb and forefinger. Stereoscopic lateral and either single or stereoscopic postero-anterior projection views are advised, the patient's head being well hyper-extended in the lateral view to give better visualization of the retro-mandibular region.

Blady, J. V., and Hocker, A. F. (1939) *Radiology*, **32**, 131.

PELLAGRA

See also Vol. IX, p. 468, and Cumulative Supplement, Key No. 1228.

Clinical Picture

Biochemical Changes in Blood

R. W. Vilter, *et al.* found that the blood of normal persons on well-balanced diets supported growth of *B. influenzae* to a much greater extent than the blood of pellagrins on diets deficient in the pellagra-preventing factor. After nicotinic acid treatment, the blood of these pellagrins increased to normal growth-promoting activity, showing that after nicotinic acid treatment coenzyme (cozymase or coferment) is increased in the blood of these patients. These observations supported the hypothesis that the therapeutic value of nicotinic acid depends on the synthesis of nicotinic acid nucleotide and finally coenzyme in the body. They also showed that the administration of riboflavin is beneficial to certain pellagrins in relapse. A liberal and well-balanced diet should always be recommended in pellagra.

Vilter, R. W., Vilter, S. P., and Spies, T. D. (1939) *J. Amer. med. Ass.*, **112**, 420.

Treatment

Nicotinic Acid

T. D. Spies *et al.* reported on the treatment of 73 pellagrins and 199 persons with subclinical pellagra by nicotinic acid, nicotinic acid amide, and sodium nicotinate. The patients treated had characteristic lesions of the mucous membrane and many had pellagrous dermatitis. After adequate dosage the glossitis, stomatitis, vaginitis, urethritis, and proctitis disappeared; the early erythemas were blanched and porphyrinuria decreased or ceased. Coramine, a diethyl amide of nicotinic acid, had similar properties. The early and late mental symptoms improved dramatically. Relapses in patients with subclinical pellagra might be prevented by daily doses of nicotinic acid. To 36 children with acute manifestations of this condition 10 doses each of 10 mg. of nicotinic acid were administered orally each day. The oral method was also strongly recommended for adults. The pharmacologically large doses of the drug acted as a powerful vasodilator and sudorific. Unlike acetylcholine it is not destroyed by passage through the capillaries. Nicotinic acid was regarded as one of the nutritional substances essential for the normal functional activity of the gastro-intestinal tract, the skin, the nervous system, and probably other organs. Pellagra was the reaction of the body to the lack of such substances. The necessity for these was increased by infection, pyrexia, or physical exercise. The dosage of nicotinic acid and its compounds required for any given case of pellagra varied widely but 500 mg. a day in divided doses was usually effective, though smaller doses often produced dramatic changes and sometimes double this dose seemed more effective. Effective treatment of any co-existing disease was of great importance.

Ten cases of pellagra were selected for study by V. H. Musick to test the efficacy of nicotinic acid therapy. Nine had a symmetrical dermatitis conforming to the Golberger type. Diet and environment were unchanged and nicotinic acid was the only adjuvant treatment employed. The author found that nicotinic acid in doses varying from 50 to 500 mg. daily is specific in curing the acute dermatitis and glossitis of pellagra and that the prolonged use of 150 to 500 mg. daily will cure the chronic dermatitis and chronic glossitis associated with the condition. Comment is made on the fact that the general health of the pellagrous patient is only slightly enhanced by treatment with nicotinic acid, and it is concluded that possibly other factors are necessary to effect a complete cure. Similar doses partially check the diarrhoea but are not effective in removing the neuritic or mental symptoms.

R. S. Matthews also reported favourable results from nicotinic acid therapy in pellagra and quoted 13 cases which benefited greatly. He emphasized the rapid healing of lesions in the alimentary tract with consequent recovery of appetite and stimulation of gastro-intestinal function. Nicotinic acid did not benefit the peripheral neuritis associated with pellagra. Intravenous and intraspinal vitamin B₁ in large doses were necessary to produce rapid improvement. Nicotinic acid considerably reduced the length of stay in hospital of severe cases.

P. Manson-Bahr and O. N. Ransford described a vitamin B₂ deficiency without any manifestation of pellagra except inflammation of the alimentary tract with stomatitis and chronic diarrhoea, glossitis, epithelial denudation, excoriations at the angle of the mouth and sometimes leucoplakia of the lower lip. This pre-pellagrous state responded well to nicotinic acid. A case was recorded of a woman, aged 62, with these symptoms for 5 years, who was completely cured by a full diet and 150 mg. of nicotinic acid daily.

I. Katzenellenbogen recorded further observations on the endemic stomato-glossitis in Palestine which he described in 1928. In the present communication an account was given of the treatment of 24 cases (18 males, 6 females) by small doses (50 mg. tablets 4 to 6 times daily) of nicotinic acid. The clinical picture of these cases resembled that in the acute phase of pellagra, but the patients did not show any manifestation of pellagra other than the glossitis. Striking improvement followed this treatment in 21 of the cases. The glossitis was regarded as due to deficiency of nicotinic acid.

Mode of Action of Nicotinic Acid

S. Petri *et al.* made a preliminary report on their experiments with gastrectomized pigs. The animals developed symptoms similar to those of pellagra. Nicotinic acid in doses corresponding to those given in human pellagra did not have any effect. As pellagra produced in pigs by Chick's diet responded well to nicotinic acid treatment, it appeared that the effect of nicotinic acid depended upon the presence of an



Pellagra rash in patient aged 15. A. Before treatment. B. After treatment with laroestidine.
(From *Journal of Tropical Medicine and Hygiene*, 1938)

PLATE V

'antipellagrous' function of the stomach. Further proof of this assumption was that, in a pig in which part of the stomach (fundus and cardia) was left, the pellagrous symptoms disappeared after nicotinic acid treatment

Amino-Acids

A recognized aetiological factor in pellagra is a deficiency of amino-acids. The periods of treatment necessary with amino-acids is shorter than that required with nicotinic acid and diet therapies. Soliman Azmy Pasha treated 6 patients, 3 with laurostidin and 3 with histophan (containing tryptophane and histidine). All the patients had the typical recurrent rash on the legs, arms, forehead, and chest. In 5 patients the rash cleared up within 21 days (see Plate V), but in the sixth and most severe case it took about 5 weeks. All cases did not receive any treatment for pellagra other than the injection of amino-acids. In 3 of the cases treatment was given simultaneously for bilharziasis and ankylostomiasis with tartar emetic and carbon tetrachloride.

Synthetic Nicotinamide

W. W. Kühnau employed synthetic nicotinamide (the amide of β -pyridinecarboxylic acid) in human pellagra. In 2 patients, one male, and one female, he injected 0.1 g. of the drug daily, and after 2 weeks the skin eruptions disappeared, but the psychical symptoms persisted. In a third, a female patient without skin eruptions, the psychical condition was unaffected. It was concluded that the reason why there was not any response in the psychical symptoms was that the disease was of some years' duration, and that early treatment by the drug was important.

Liver Extract

Because failure of hepatic function or of storage of an essential substance in the liver has been suspected to be a factor in the causation of pellagra, and, as analogies have been drawn between pellagra and pernicious anaemia, V. P. Sydenstricker *et al* tested the efficacy of an extract of the liver of a patient dying with acute and untreated pellagra on patients with the above 2 diseases. The liver extract, prepared by Cohn's method, was given intravenously to 2 patients with endemic pellagra, who did not show any improvement. A patient with typical pernicious anaemia treated in the same way gave a prompt and good reticulocyte response with a subsequent increase in red blood-cells and the haemoglobin content. It therefore appeared that extract of liver in pellagra was rich in the haemopoietic factor, but totally lacking in the pellagra curative substance present in commercial liver extracts. Further, these observations suggested the existence of a factor, other than nicotinic acid, which was active in the cure of pellagra and present in normal mammalian liver and in its refined extracts but absent from the liver in pellagra.

Azmy, S. (1938) *J. trop. Med. (Hvg.)*, **41**, 357.

Katzenellenbogen, I. (1939) *Lancet*, **1**, 1260.

— (1928) *Arch. Derm. Syph., Wien*, **154**, 269.

Kühnau, W. W. (1938) *Med. Klinik*, **34**, 1088.

Manson-Bahr, P., and Ransford, O. N. (1938) *Lancet*, **2**, 426.

Matthews, R. S. (1938) *J. Amer. med. Ass.*, **111**, 1148.

Musick, V. H. (1939) *Amer. J. digest. Dis.*, **5**, 807.

Petri, S., Nogaard, F., and Bandier, E. (1938) *Acta med. scand.*, **98**, 117.

Spies, T. D., Bean, W. B., and Stone, R. E. (1938) *J. Amer. med. Ass.*, **111**, 584.

Sydenstricker, V. P., Schmidt, H. L., Jnr., Geeslin, L. E., and Weaver, L. (1939) *Amer. J. med. Sci.*, **197**, 755.

PEMPHIGUS AND PEMPHIGOIDS

See also Vol IX, p. 482.

Pemphigus Vulgaris

Treatment

Calciferol.—H. King and C. M. Hamilton reported the case of a male patient, aged 65, who exhibited a wide-spread pemphigus vulgaris. His condition became

grave, and after 5 months of varied treatment he was rapidly losing ground. At this stage massive doses of vitamin D were administered in the form of calciferol in capsules, each containing 50,000 U.S.P. units of vitamin D; 300,000 to 400,000 units per day were given for 3 or 4 weeks. This dosage greatly improved the skin lesions but resulted in nausea, epigastric distress, mental apathy, and general weakness. The dose was reduced to 100,000 units a day and was kept at that figure for a year. The patient remained free from cutaneous lesions and symptoms of hyper-vitaminosis. Eleven months after the treatment had been discontinued there was no recurrence, nor had any untoward effects resulted from it.

Germann—C. C. Tomlinson and O. J. Cameron discuss the varying results obtained from the use of germanin in pemphigus. Its results have not been consistent. Reports of 3 cases of juvenile pemphigus are included, each of which was treated with germanin when all other treatments had failed. Two of these were apparently cured, but the third, which received a second course, died 10 weeks after the last injection, death was due to atrophy of the adrenal cortex. It is pointed out that dosage must be adjusted to the patient's tolerance. The initial dose for an adult should be 0.5 g. with subsequent doses of 1 g. every other day for another 4 doses, providing toxic signs such as albuminuria, fever, and toxic erythema do not appear. Not more than 5 injections at intervals of 2 days should be given in any one course. During this treatment, daily urinalysis and estimations of blood pressure should be made. Frequent blood counts with estimations of the non-protein nitrogen content of the blood and the potassium, sodium, and chloride contents should be made, in order that degeneration of the adrenal cortex may be detected early.

Serum from bullae—Acting on the report of Urbach and Wolfiam (1936) that the blood-serum of patients with pemphigus contained antibodies specific to the antigen present in the skin bullae, S. Watson Smith treated a case of pemphigus of several weeks' standing, by intramuscular injections of serum extracted from the bullae and treated with 0.05 phenol for 24 hours, the dosage varying from 0.5 c.c. to 1 c.c. Local treatment consisted in the application of oil and chalk lotion to the eruption twice daily. No dressings were needed. Great improvement followed with total disappearance of the eruption.

King, H., and Hamilton, C. M. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 515.

Smith, S. W. (1939) *Brit. J. Derm.*, **51**, 213.

Tomlinson, C. C., and Cameron, O. J. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 555.

Urbach, and Wolfiam (1939) *Arch. Derm. Syph., N.Y.*, **33**, 788.

Ocular Pemphigus

F. L. P. Koch reported a case of chronic ocular pemphigus in a man aged 54. The symptoms included gradual reduction of vision in both eyes of about four months' duration, associated with a slow thickening of each lower lid, which had become adherent to the lower portion of each globe. There was also a reddened area along the gum line below the lower front teeth, with tenderness of the mouth and slight sore throat. Examination revealed—V.A. (with glasses) R 1/6 15, L 1/6 20. Near vision had been reduced to the ability to read 14/35 (American Medical Association rating). The erythematous and thickened palpebral and bulbar conjunctiva presented a moderately uneven surface which was studded with irregularly rounded and elongated, slightly elevated, glistening grey patches. Two small, characteristic, red bullae, typical of ocular pemphigus, were observed in the middle third of the right lower lid near the palpebral-ciliary margin. These were 2 mm. in width, 1 mm. in height, and 4 mm. in length, and they ruptured in a few hours. No bullae were ever observed in the left eye. Local treatment consisted of the use of a 2 per cent boric acid solution, followed by 0.5 per cent pontocaine hydrochloride drops. Vitamin A (10,000 units per gram) ointment was placed in both fornices of each eye. This treatment was administered daily for 21 days. The patient's general condition was treated by the administration of sulphanilamide, 10 grains being given orally 3 times a day for a week.

Koch, F. L. P. (1939) *Amer. J. Ophthalm.*, **22**, 298.

PENIS AND SCROTUM DISEASES

See also Vol. IX p. 498.

Priapism

H. L. J. Defesche discussed priapism. This condition is often extremely painful and there is no ejaculation to relieve the turgor. Micturition is quite painless, in contrast to physiological erection. Priapism is serious not only on account of its pathology but also because of the psychic damage it can cause. The author explained a few general points in the diagnosis of priapism, absence of cerebral lesions and of ischio-cavernosus contractions and acute exacerbation after sexual exertion denote a mechanical origin, which is further diagnosed by the persistence of the condition for more than a week. If the condition is of nervous origin large doses of sedatives are essential, and in cases lasting over a fortnight surgical intervention is necessary. Unilateral or bilateral incisions are made into the cavernous tissue and the hardness gives place to a normal penis.

Defesche, H. L. J. (1939) *J. Urol. méd. chin.*, **47**, 465

Thrombophlebitis*Aetiology and Treatment*

Ten cases of thrombophlebitic lesions of the penis were reviewed by M. R. Keen and S. Shlimbaum. The aetiology of these cases varied, the commonest causes being: (i) malignancy of the left kidney, because the spermatic vein entered the left renal vein at right angles and any tumour involvement of the renal vein or artery obstructed the return flow from the penis and scrotum, (ii) leukaemia, which favoured thromboses in blood spaces such as the corpora cavernosa, (iii) arteriosclerosis; (iv) sexual excesses in the presence of local varicosities, and (v) infection, either local, such as gonorrhoea, or systemic. A case of extensive thrombosis of the penis and scrotum was reported in a 20-year-old male, apparently secondary to an upper respiratory infection. The treatment of the condition varied with the aetiology. If infection was present simple wet dressings on the part sufficed. When arteriosclerosis was an associated factor absorption of the clot might occur spontaneously or with potassium iodide administration. In some cases it might be necessary to incise the corpora and evacuate the clot. In leukaemia irradiation of the penis was beneficial.

Keen, M. R., and Shlimbaum, S. (1938) *Amer. J. Surg.*, **41**, 228

Carcinoma*Treatment*

Surgical and radiotherapeutical — C. J. Hansson gave an account of cases of cancer of the penis treated with combined radical surgical and radiotherapeutical methods. The results were promising. Of 106 patients seen between 1912 and 1937, 73 were treated; they were divided according to the clinical condition of the lymphatic glands at the beginning of treatment into 3 stages: (i) without clinically demonstrable metastases in the lymphatic glands, 45 cases, of which 15 were suspected to have glandular involvement but were shown histologically to be inflammatory lymphadenitis, (ii) with clinically positive lymphatic glands; 16 cases, the cancer being localized (operable), and (iii) 12 cases, all advanced with metastases in the lymphatic glands and further distribution of the cancer (inoperable).

In all stages radiotherapy alone gave unsatisfactory results; the growth, usually a highly differentiated keratinized squamous-celled carcinoma, was of relatively low radio-sensitivity; it was generally infected; and the normal tissues of the penis were prone to necrosis. The combined treatment was as follows. Stage I. Electrocoagulation or, if recurrence was suspected, amputation. Inguinal lymphatic nodes were treated with X-rays or telerradium. There were 85 per cent of 5-year cures. Stage II: Amputation, and X-ray or telerradium treatment of the lymphatic glands. If after 2 months there were still metastases in the lymphatic glands, they should be dissected out. There were 58 per cent of 5-year cures. Stage III. If it could be carried through tissue free from cancerous infection, amputation of the penis should be performed, as it might provide a palliative result by partially reducing the infection of the lymphatic glands or by relieving the pain and difficulty in micturition. If the

cancer extended in continuity from the primary tumour to the metastases, amputation was futile. Metastases in the lymphatic glands could be treated by fractional external irradiation in small daily doses. None of the patients in Stage III survived for 5 years.

Hansson, C. J. (1938) *Acta radiol., Stockh*, **19**, 443.

PEPTIC ULCER

See also Vol IX, p 504, and pp 46 and 167 of this volume

Aetiology

Incidence

G. Alsted, from analysis of the records of Copenhagen, found that during the last 50 to 60 years the following changes had taken place in regard to peptic ulcer. Both in males and females acute ulcer of the body of the stomach had become less frequent, and peptic ulcer had moved from the lesser curvature of the stomach to the pyloric region or the duodenum. Peptic ulcer, formerly more frequent in women, was now more often seen in men and haemorrhage was now more often seen than formerly.

Vitamin B deficiency

Investigations to determine the relation of vitamin B deficiency to peptic ulcer were carried out by M. N. Rao. The presence of pyruvic acid in the blood may be taken as a fairly accurate test for avitaminosis B. In the 30 cases under review modified MacLean's and Cook's methods of estimating the amount of pyruvic acid present were used. The first is effected by the precipitation of pyruvic acid with phenyl hydrazine and subsequent estimation of unchanged hydrazine. By the second method the pyruvic acid is estimated as an unknown quantity of the bisulphite-binding substances in the blood. A definite increase in the bisulphite-binding substances in the blood of peptic ulcer cases was found, revealing a marked deficiency in the vitamin B of these patients. The normal average value of bisulphite-binding substance is given as 4.8 whereas values shown by peptic ulcer cases in this series ranged from 2.1 to 23.73.

Psychogenic Disturbances

A. Winkelstein and A. A. Berg comment on the fact that to-day there is a strong tendency to regard a psychogenic disturbance as the cause of peptic ulcer, the nervous pathway being the vegetative nervous system, and chiefly the vagus, which increases motor and secretory activities. The authors discuss the acidity of peptic ulcer patients both before and after partial gastrectomy. In order to avoid a recurrent ulcer after this operation, achlorhydria is the ideal state, and subphrenic anterior vagotomy in addition to a partial gastrectomy will produce an achlorhydria in most duodenal patients with a very high pre-operative acidity.

Factors causing Variations in Gastric Acidity

F. Hollander reviewed the numerous factors which might be responsible for variations in the gastric acidity, dividing the factors into extra-gastric and intra-gastric. Among the extra-gastric were (i) dilution by the test-meal, (ii) dilution and neutralization by the saliva, and (iii) dilution and neutralization by regurgitated duodenal fluid. The intra-gastric factors included (iv) possible variations in the composition of the secretion of the parietal (oxyntic) cells, (v) reabsorption of hydrochloric acid already secreted, by the gastric mucosa, (vi) dilution by the peptic secretion, (vii) dilution and neutralization by a distinct dilution secretion, and (viii) the diluting and neutralizing effects of mucus secreted from the surface epithelium. Of these factors the first was non-physiological and a method had been devised whereby the dilution by the test-meal could be estimated and correction made for it in future experiments, and (iv) has been found to be untenable. All the other factors merit investigation and Hollander brought forward evidence that the variations in gastric acidity were due primarily to neutralization by buffer substances, such as protein, phosphate, and alkaline bicarbonates, and to dilution by the fluids containing them.

Experimentally-produced Ulcers

F. C. Mann described 3 types of peptic ulcer which could be produced experimentally in animals. The first is multiple, superficial, and began as a sub-mucosal

haemorrhage. They rarely extend more deeply and rarely become chronic. The second type resembles the chronic peptic ulcer seen in man. It is usually single and occurs at the pylorus, never in the fundus. It begins as an acute ulcer and, unless it perforates, goes on to become chronic. The third type of ulcer begins as a gastritis involving both the pyloric and fundal mucosa. The fundal lesions heal quickly, but those in the pylorus proceed to chronic ulcers as long as the irritating agent is allowed to persist. They resemble chronic pyloric lesions in man but they are often multiple. The ulcers may be produced in 2 ways. The first consists in interference with the blood supply to the mucosa which then breaks down and forms an ulcer. The second type develops only in mucosa exposed to acid, and appears where the gastric contents first strike the mucosa. The surface mucosa is chemically destroyed by the acid and the cells are then mechanically swept away, and an ulcer forms. Succeeding layers of cells are injured, and the ulcer becomes chronic as the process progresses. As soon as the ulcer is protected from acid it heals. A few hours after removal of acid from the site of the ulcer it begins to heal by granulation, and then the mucosal epithelium grows over the granulation tissue. If the ulcer is not protected from gastric contents, destructive processes occur more rapidly than reparative ones, and it cannot heal. All the common complications of gastric ulcer occurring in man were seen in these experimental ulcers. Many of them perforated, and haemorrhage, sufficient to kill the animal, was not uncommon.

Alsted, G. (1939) *Studies on the Changing Incidence of Peptic Ulcer of the Stomach and Duodenum*, London.

Hollander, F. (1938) *Amer. J. digest. Dis.*, **5**, 364.

Mann, F. C. (1939) *Brit. med. J.*, **1**, 707.

Rao, M. N. (1938) *Indian med. Gaz.*, **73**, 457.

Winkelstein, A., and Berg, A. A. (1938) *Amer. J. digest. Dis.*, **5**, 497.

Course

W. L. Palmer *et al.* have investigated the peptic ulcer problem from the point of view of the healing process which may be either very rapid or exceedingly slow, varying in time from one month to over 2 years. Such slow rate of progress probably depends on the failure of the patient to carry out the required treatment of rest, acid neutralization, and high-calorie diet, and for this reason stay in hospital frequently improves such cases. When healing still remains a slow process even under favourable circumstances, and when the regime is faithfully followed, the slow gastric emptying time is considered responsible for the delay. When gastric emptying is slow it is usual to find the antrum of the stomach narrow, although smooth and pliable. The exact mechanism involved is not entirely clear.

Palmer, W. L., Schindler, R., and Templeton, I. I. (1938) *Amer. J. digest. Dis.*, **5**, 501.

Diagnosis

Phenolphthalein Test

A test recently reported by Woldman was utilized by D. N. Kremer *et al.* in an attempt to diagnose the presence of organic lesions in the gastro-intestinal tract. Ten c.c. of a 1 per cent alcoholic solution of phenolphthalein were given by mouth, fasting, to 137 hospital patients. The urine was tested immediately after being passed at 2-hourly and 4-hourly intervals. A sixth hour specimen was tested when the former had furnished negative results. When the urine contained free phenolphthalein, the addition of 1 to 3 drops of 10 per cent sodium hydroxide turned it pink or red. Urine without phenolphthalein did not change in colour. When free phenolphthalein was found in the urine the presence of a gastro-intestinal lesion was suspected. The test was originally evolved on the theory that the greater portion of ingested phenolphthalein is excreted unchanged in the faeces, the remainder appearing in conjugated form in the urine. Presence in the urine of free phenolphthalein was presumed to indicate a break in the mucosa of the gastro-intestinal tract. Results were correct in 56 per cent of cases with proved gastro-intestinal diseases, and in 79 per cent when there was no evidence of disease. The test was not considered satisfactory, but might be useful in conjunction with other diagnostic measures.

Kremer, D. N., Shore, P. D., and Wiesel, B. H. (1939) *Amer. J. digest. Dis.*, **6**, 192.

Complications

Secondary Changes in Central Nervous System

A. R. Vonderahe studied 14 cases of peptic ulcer, 7 duodenal, 6 gastric, and 1 gastric and duodenal, in which necropsy revealed no localized lesion of the brain. It is known that gross neurological lesions will sometimes produce gastric ulcer, the author also claimed that gastric ulcer itself produced secondary neurological effects. All cases showed congestion of the brain, either localized or generalized, and in all there were haemorrhages in the dorsal motor nucleus of the vagus, the nucleus reuniens complex of the thalamus, and the anterior portion of the hypothalamus. The author considered these changes were secondary to specific localized vaso-motor effects due to intense local functional activity and strong afferent stimulation. He thought that many of the 'neurotic' sequelae of peptic ulcer, such as ascending pulse rate, hyperidrosis, signs of sympathetic imbalance, fatigability, emotional changes, disturbances of sleep, and alterations in metabolism might be due to these haemorrhagic lesions.

Vonderahe, A. R. (1939) *Arch. Neurol. Psychiat., Chicago*, **41**, 871

Treatment

Colloidal Aluminium Hydroxide

Treatment with colloidal aluminium hydroxide is recommended by R. B. Rutherford and F. S. Imery for those peptic ulcer patients with marked hypersecretion whose symptoms are not relieved by other medical treatment, and for those with post-operative jejunal ulcer. It is also useful in cases of peptic ulcer associated with nephrolithiasis. Alkalosis does not develop following its use. It is administered by the continuous drip method for 7 days and nights at the rate of 15 drops per minute. The patients are also given 90 c.c.m. of equal parts of milk and cream every hour and supplementary feedings are gradually introduced. At the end of a week the antacid is discontinued for 24 hours and a gastric analysis performed and compared with one taken prior to commencement of treatment. If the gastric acidity is not markedly lower the treatment is resumed for another week. When a drop in acidity is shown, the drip treatment is discontinued and 60 c.c.m. of diluted colloidal aluminium hydroxide are given every hour from 8 a.m. to 9 p.m. by mouth. Twenty-eight patients treated with colloidal aluminium hydroxide obtained relief from pain in 24 hours. Of these 18 underwent the treatment described and 10 were ambulatory patients treated orally. In the latter a longer period was necessary to obtain low acid levels.

M. M. O'Brien also reported 2 cases of peptic ulcer successfully treated by administration of colloidal suspension of aluminium hydroxide by the continuous drip method. The apparatus for its administration consisted of a number 10 Levin tube, 2 bottles, a water reservoir, and connexions. The Levin tube was passed through the nose down to the lower end of the oesophagus, and was then connected with a bottle from which was siphoned a 5 per cent colloidal suspension of aluminium hydroxide (amphojel) which was diluted with 3 volumes of water and allowed to run in at the rate of 6 to 8 drops per minute. The intubing tube caused very little discomfort. It had been shown that aluminium was not absorbed into the blood. The great disadvantage of medical antacid treatment, apart from the danger of alkalosis, had previously been its intermittency, especially its discontinuance during the long night period. The continuous drip method kept the gastric contents and juice neutral throughout the whole 24 hours. The amount of hydrochloric acid secreted was much diminished, but the secreting cells were not damaged, for, even after prolonged treatment by this method, the response to injection of histamine was normal. In most cases complete healing of the ulcer might be expected in 7 to 14 days.

T. Izod Bennett and A. M. Gill investigated a group of patients to determine the value of aluminium hydroxide gel in the treatment of peptic ulcer. They considered: (i) that it possessed, in doses of 1 to 3 fluid drachms, antacid powers as great as those of ordinary doses of alkaline powder; (ii) that it did not produce an alkalosis even when given in amounts of 3 to 4 fl. oz. in 24 hours, and (iii) that, when substituted for alkaline powder to aid the dietetic treatment of proved peptic ulcer, it was preferred by patients and was even more effective in banishing symptoms. It had the additional value of not setting up diarrhoea, which is often a troublesome feature of alkali treatment. The chief claim made for aluminium hydroxide gel is that, having amphoteric qualities, it neutralizes hydrochloric acid in considerable quantities without

becoming basic; it is claimed that this substance combines with hydrochloric acid to form aluminium chloride, and that in the small intestine the biliary and pancreatic juices react with it to re-form sodium chloride and reprecipitate aluminium hydroxide.

Magnesium Trisilicate

Investigations into the treatment of peptic ulcer with magnesium trisilicate led C. J. Tidmarsh and R. G. Baxter to conclude that, providing the preparation was chemically pure and of a definite standard, it was of considerable value. Of 26 patients with duodenal and gastric ulcers treated by this means, only 3 responded unfavourably. One of them was found to have an ulcer penetrating deeply into the pancreas; the other 2 in spite of the improvement of their gastric symptoms suffered from intractable diarrhoea. Treatment consisted of 35 gr. of magnesium trisilicate, administered 6 times a day. This was reduced to 4 doses daily after the severe symptoms had disappeared, usually in 4 to 8 days. Treatment was continued until radiographs showed no evidence of ulcer, usually after 4 to 6 weeks. A bland diet with 2-hourly feeds supplemented this therapy. Magnesium trisilicate appears to be an efficient non-toxic antacid which rarely disturbs the motility of the gastrointestinal tract and produces no general side reactions.

M. Kraemer used magnesium trisilicate on 38 patients with definite duodenal ulcers for a period of 3 to 6 months. Three light meals a day were allowed, and in addition a glass of milk between meals and in the evening. One hour after meals and after the between-meals feed, and at bedtime, they received a teaspoonful of hydrated magnesium trisilicate powder. If nervous or sleepless, bromide or phenobarbitone was given. In order to eliminate any psychic effect, these patients were not told of the alteration in treatment. They all showed improvement. The author states that magnesium trisilicate is not curative, but is a valuable antacid, which even in large doses produces no diarrhoea, constipation, or alkalosis.

Insulin

M. Roller treated 8 cases of duodenal ulcer, 7 cases of gastric ulcer, and 14 cases of chronic gastritis with insulin. During the early days of treatment, no meat was given, otherwise the diet was on ordinary lines. Subcutaneous injections of 10 to 15 units of insulin 3 times daily were given for 3 to 4 weeks, and after a few days gastric pain ceased. But, if pain persisted, 15 to 20 units of insulin, in addition to the daily dose, should be injected for a few days. A series of X-ray examinations showed complete cure of the ulcer after 3 to 4 weeks of insulin treatment, and other drugs were unnecessary. Acid content of the gastric juice was unaltered. The dosage of insulin must be decided by the individual's requirements, usually 10 units in the morning, and 15 to 20 units at midday and at night were suitable. In insulin-sensitive patients the daily total should not exceed 25 units, and sometimes the dose had to be reduced to 5 units 3 times a day. Any signs of over-dosage should be met by giving biscuits or tea with sugar. After completion of the treatment the patient should take a mixed diet rich in carbohydrates and should not have more than 3 meals a day so as to obviate any tendency to eat too much.

Surgery in Obese Subjects

W. Walters and O. T. Clagett state that, although the presence of obesity might make the operative treatment of gastric and duodenal ulcers difficult, it is not a contra-indication to surgery. They reported 11 cases of successful operation. In most of these partial gastrectomy was performed with an anastomosis posterior to the colon. An anterior anastomosis may be necessary in an obese patient with a thick, heavy, fat mesocolon. If a long loop of jejunum has to be used to make the anterior anastomosis, it may be necessary to establish an entero-anastomosis to prevent accumulation of fluid and gastric retention in the long proximal loop of the jejunum. After posterior anastomosis the obese patient may develop gastric retention and it is necessary to introduce food through a jejunostomy tube until the inflammation at the anastomosis or in the transverse mesocolon has subsided.

Prognosis after Partial Gastrectomy

J. Morley and F. H. Bentley examined 67 cases of partial gastrectomy with an average interval of 8½ years since operation. Of the patients, 58 had undergone a Schoemaker gastrectomy and 9 a Polya gastrectomy. Each patient was investigated by fractional gastric analysis. The gruel test meal was used and supplemented by histamine injections, so that the stomach might have the maximal acid-secreting

stimulus. In the Schoemaker cases, gastric activity was abolished in nearly one-half, depressed in almost one-third, and normal in about a quarter. In the 9 Polya gastrectomies, no free acid was demonstrated in any case. The diminished acid values after partial gastrectomy are mainly due to simple dilution and neutralization, which is accompanied by free regurgitation of bile and rapid emptying of the stomach. When gastric activity was severely depressed, there was a high incidence of microcytic anaemia possibly due to interference with the absorption of iron caused by the absence of free acid. When this activity was not depressed, there was a risk of further ulcer symptoms. The depression of activity being less severe after Schoemaker's gastrectomy, the incidence of anaemia was correspondingly less.

Late Results of Surgical Treatment of Perforation

J. Verney Cable reported on the subsequent histories of 24 cases operated on for perforated peptic ulcer at Wellington (N.Z.). The treatment in all cases was simple closure. The investigations were made at a period after the operation varying from 6 months to 3½ years. In 2 cases patients were completely free from symptoms and could eat anything. Six retained good health and could eat anything subject to some dietary restrictions. Six had trouble, even on a modified diet, but were able to continue work. In 10 patients the results were poor; of these 4 had surgical treatment, from which 2 died, and 2 have since died from gross haemorrhage, 2 more were readmitted to hospital, one with pyloric stenosis and in a poor general condition. These figures, which admittedly are small, do not lend any support to the view that a considerable proportion of cases of perforated ulcer are free from symptoms after surgical suture.

Bennett, T. I., and Gill, A. M. (1939) *Lancet*, **1**, 500.

Cable, J. V. (1938) *Brit. med. J.*, **2**, 403.

Kraemer, M. (1938) *Amer. J. digest. Dis.*, **5**, 422.

Morley, J., and Bentley, F. H. (1938) *Brit. med. J.*, **2**, 645.

O'Brien, M. M. (1938) *Med. J. Aust.*, **2**, 559.

Roller, M. (1938) *Med. Klinik*, **34**, 1129.

Rutherford, R. B., and Emery, I. S. (1939) *New Engl. J. Med.*, **220**, 407.

Tidmarsh, C. J., and Baxter, R. G. (1938) *Canad. med. Ass. J.*, **39**, 358.

Walters, W., and Claggett, O. T. (1939) *Proc. Mayo Clin.*, **14**, 261.

Multiple Perforating Ulcers

W. I. Austin referred to the 32 authentic cases of multiple perforated ulcers analysed by Mason and Simon. Of these 18 had a laparotomy performed but in only 4 cases were both perforations closed, these 4 patients survived. The author recorded a fresh case of a man aged 27, who had simultaneous perforation of a gastric and a duodenal ulcer (see Fig. 19). Both were closed by Lambert sutures and the patient made an uneventful recovery.



FIG. 19—Diagrammatic representation of pyloro-duodenal region, showing the position of the ulcers, one on the lesser curvature of the stomach and the other on the anterior wall of the duodenum near the pylorus. (From *The British Journal of Surgery*, 1939)

Austin, W. E. (1938) *Brit. J. Surg.*, **26**, 387.

PERONEAL MUSCULAR ATROPHY

See also Vol. IX, p. 565

S. M. Small and A. T. Milhorat reported 7 cases of peroneal muscular atrophy in 3 generations of one family. One patient showed defects of sensory perception, and another's condition resembled chronic progressive anterior poliomyelitis. The other 5 patients showed the usual clinical manifestations of the disease. The hereditary factor in the family appeared to be dominant, and one or more descendants of all the affected parents showed definite evidence of the disease. It has been shown that, in muscular wasting following involvement of the nervous system, the diminution in the output of creatinine is related to the reduction in the amount and efficiency

of the total muscle mass. The metabolism of creatine and creatinine in 4 of these patients was investigated, and showed very little alteration in spite of the involvement of important muscle groups. The explanation given for this was that normal persons excrete such large quantities of creatinine that the small reduction that might result from muscular loss was not appreciated.

Small, S. M., and Milhorat, A. T. (1938) *Arch. Neurol. Psychiat.*, Chicago, **40**, 911.

PHARMACOLOGY

Adrenaline

J. V. Galgiani *et al* investigated the local and systemic effects of the inhalation of a strong solution of adrenaline. Experimenting with cats they found that the adrenaline was not absorbed from the respiratory tract unless it had been inhaled deeply into the lungs. Absorption from these caused a rise of blood pressure even in minute doses. Inhalation of a 1 per cent solution caused irritation and inflammation of the tracheal mucosa. These changes were also found in a tuberculous patient who had inhaled 1 per cent adrenaline for 48 hours before death.

Galgiani, J. V., Proescher, F., Dock, W., and Tainter, M. L. (1939) *J. Amer. med. Ass.*, **112**, 1929.

Areca

H. Schlegel discussed the use of areca seeds as an anthelmintic as it was found that many 'patent' medicines contained areca instead of santonin. It was found that the pharmacopoeias of European countries, with the exception of the Swiss pharmacopoeia, did not specify a maximal dose. The principal constituent of the drug is the alkaloid arecoline, the maximal dose of hydrobromide being 0.0005 to 0.0015 g. The author warns against the excessive use of this drug, and points out the desirability of putting preparations containing arecoline on the Poisons List.

Schlegel, H. (1939) *Arch. exp. Path. Pharmac.*, **192**, 389.

Atebrin

Relation of Toxic Manifestations to Dosage

The acute lethal oral dose of atebrin for cats, rabbits, and mice has been reckoned as between 0.3 and 1.0 g. per kilogram of body weight, according to the animal. The lethal dose for dogs has been considered to be slightly above 0.3 g. per kilogram. Experiments were performed by S. J. Martin *et al* to ascertain the effect of chronic daily medication in dogs, cats, and rabbits, and it was found that a daily dose exceeding 3 per cent of the acute lethal dose continued for 47 consecutive days caused a 16 per cent loss in body weight. Dogs receiving 0.1 g. of atebrin per kilogram, which was about 33 per cent of the minimal lethal dose, showed manifestations of salivation, anorexia, vomiting, diarrhoea with blood in the stools, progressive loss of weight, weakness, and a yellowish discoloration of the mucous surfaces of the mouth and the vagina. On the average, death occurred in these dogs on the nineteenth day. The same symptoms appeared earlier when the dosage was 0.2 g. per kilogram, or 66 per cent of the minimal lethal dose, and there was terminal excitation of the central nervous system with convulsions and respiratory paralysis, death occurred in 4 days. Symptoms in cases in which the dosage was 0.5 g. per kilogram, or 17 per cent of the minimal lethal dose, were mild gastro-intestinal disturbances and depression of the central nervous system. Experiments with cats and rabbits showed that symptoms were similar but less severe. It was concluded that the toxic manifestations which followed routine administration of atebrin depended on the dosage employed. Excretion or destruction of the drug never exceeded 85 per cent in the case of the larger doses. Necropsy findings revealed no changes peculiar to atebrin toxicity, with the exception of yellowish discoloration of the mucosa of the gastro-intestinal and urinary tracts. This discoloration was also observed on section of the liver, spleen, pancreas, and kidney.

Martin, S. J., Cominole, B., and Clark, B. B. (1939) *J. Pharmacol.*, **65**, 156.

Benzedrine Sulphate

Effect on Gastric and Intestinal Activity

K. H. Beyer and W. J. Meek studied the effect of benzedrine sulphate on gastric and intestinal activity in man, by means of X-ray examinations of 10 normal students divided into 3 groups, and to avoid the possibility of cumulative effects of X-rays no group was used more often than once in 3 weeks. Benzedrine decreased the time of initial emptying of the stomach to about 42 per cent of the normal and prolonged the time for final emptying by 21 per cent. On dogs' stomachs benzedrine given orally in solution exerted a twofold action; the initial response usually occurred 8 minutes after the drug was taken, namely, increased rate, tonus, and amplitude of gastric contractions, resulting in a rise of intragastric pressure. After about 40 minutes, a second and now inhibitory phase followed, which usually lasted more than an hour. The drug, even in toxic doses, had not any demonstrable effect on the animal intestine *in situ*. On isolated intestinal strips and with a concentration of drug higher than could be obtained in the normal animal, the most constant effect of benzedrine was a decrease in tonus. The tonus of the pylorus, on the other hand, appeared to be increased by benzedrine. Its effect in decreasing the initial emptying time of the normal stomach and in overcoming moderate functional pylorospasm must therefore be due to increased intragastric pressure rather than to any direct inhibiting effect on pyloric tonus.

Beyer, K. H., and Meek, W. J. (1939) *Arch. intern. Med.*, **63**, 752.

Chamomile Flowers

W. Heubner and W. Albath examined the properties of the different constituents of German chamomile flowers (*Matricaria Chamomilla*), and found that, besides their other actions, they have a definite anti-inflammatory effect. This was found to be due to the constituent azulene $C_{15}H_{18}$, which was isolated by precipitation from the oil with hydroferrocyanic acid.

Heubner, W., and Albath, W. (1939) *Arch. Path. Pharmacol.*, **192**, 383.

Curare

Curare blocks the nerve impulse at the myoneural junction and causes peripheral paralysis. The injection of curare reduces spasm and plastic muscular rigidity in patients with spastic paralysis and other conditions. The curine present in the curare produces headaches and vertigo about 30 minutes after injection, accompanied by a fall of blood pressure. Lateral nystagmus occurs in some cases. From 5 to 10 minims of adrenaline solution counteracts these toxic effects. M. S. Burman gave curare to 19 patients suffering from spastic paralysis. The drug was given either intramuscularly, in doses of from 10 to 40 mg., or intravenously, in doses of about 25 mg., and relieved the spasm and rigidity. Orthopaedic surgery and muscle training must be used in conjunction with the drug. The duration of the effect of the curare varies usually from 1 to 2 days, but may last as long as 12 days. It is possible to use the drug like insulin, starting with a small dose and then establishing a stabilizing dose. If the drug is self-administered, a careful watch must be kept for toxic signs, as serious asphyxia may result. Heaviness of the eyes and smoothing of the face, which assumes a stupefied expression, are toxic signs to be looked for while the injection is being given.

Burman, M. S. (1939) *Arch. Neurol. Psychiat., Chicago*, **41**, 307.

Curarine and Eserine

Antagonistic Effects

Experimenting with different types of mammalian muscle, G. Briscoe found that, in muscles poisoned by drugs of the eserine group, slow rates of stimulation produced larger contractions than fast rates. In the slow-rate myogram, the depressant effect of the eserine could be temporarily relieved by repeated activity of the muscle. In mild curarine poisoning there was no reversal of grading, faster rates producing larger contractions than slow ones, but the magnitude and power of maintaining the contraction were reduced. In more severe poisoning the responses to all rates were twitch-like small contractions. The antagonistic action of curarine to eserine was shown by curarine restoring the normal response to all rates of the muscle poisoned by eserine. If the dosage was correct this rectification was permanent; if it was too

large it was followed by depression of the curarine type. It has been suggested that curarine opposes eserine by raising its threshold for depressant action.

Briscoe, G. (1938) *J. Physiol.*, **93**, 194.

Ergometrine

Ergometrine given orally causes contractions in the human puerperal uterus similar to those produced by the liquid and solid extracts of ergot. It acts more quickly than other alkaloids, being less liable to cause headache and vomiting. A. D. McLachlin studied its action on isolated strips of muscle from the uteri of guinea-pigs and rabbits, and from the pregnant and non-pregnant human uterus. It was found that rhythmic contractions were induced in the quiescent uterus, but that ergometrine appeared to have little effect on muscle which was already contracting. In the isolated human uterus there was no evident increase in activity in the rhythmically contracting material. The results obtained would not have led to the conclusion that ergometrine possessed the already recognized property of causing contractions in the human post-partum uterus. The difficulty of showing the action of the drug on isolated strips of muscle suggested that its action on the uterus was not entirely peripheral. The action of adrenaline on the uterus and Fallopian tubes was reversed by ergometrine.

McLachlin, A. D. (1938) *J. Pharmacol.*, **64**, 243.

Hypertonic Solutions

Effect on Kidneys

Hypertonic solutions, such as salt and sugar, are often used in clinical practice, and H. A. Lindberg *et al.* investigated their effect upon the kidneys. They found, in a series of 15 cases, that 200 c.c. of a 50 per cent solution of sucrose given intravenously produced no impairment of renal function in man and failed to aggravate any existing impairment. In dogs, injected with comparable doses, there resulted transitory glomerular changes which were most marked 3 to 5 days after injection, and it was only after repeated injections that the damage became permanent. A 50 per cent solution of *D*-sorbitol given intravenously to dogs produced no renal changes. Similarly, even after 10 or 12 days, a 10 per cent solution of sodium chloride administered to one series of dogs, and a 50 per cent solution of dextrose to another series, produced no renal damage.

Lindberg, H. A., Wald, M. H., and Barker, M. H. (1939) *Arch. intern. Med.*, **63**, 907.

Maggots Application of Active Principle

For six and a half years S. K. Livingston and his collaborator have performed laboratory and clinical research on the 'active principle of maggots'. It was found that a greaseless paste or jelly was a more suitable vehicle for use in superficial lesions, such as abscesses, boils, haemorrhoids, skin lesions, and ulcers. The liquid preparation was used in cases of osteomyelitis, compound fractures, and in cervical and genito-urinary infections. The jelly, which had a 5 per cent maggot content, was used in 306 cases and was found particularly effective in those which were chronic. Healing was promoted and pain and irritation were relieved. In the treatment of abscesses a more rapid localization of the lesion occurred, thus permitting earlier surgical intervention.

Livingston, S. K. (1938) *Amer. J. Surg.*, **41**, 49.

Quinine

Fate in Body

The fate of quinine in the body is not completely established. Many authors think that about 30 to 50 per cent of the quinine remains in the body and is destroyed in various organs. In order to verify these figures, G. Lohman performed many experiments on rabbits. Twenty-eight rabbits were killed after intravenous injection of 0.10 and 0.15 g. of quinine dihydrochloride, some after 15 minutes, others after 4 hours, 24 hours, 48 hours, 72 hours, and 4 and 5 days. Analysis showed that, in the first three days, quinine was found mostly in the stomach and then in the large intestines, less was found in the small intestines and still less in the rectum.

Four days after injection quinine could not be found in the gastro-intestinal tract at all. In another experiment quinine was injected into either the small or the large intestine, or into a portion of either large or small intestine which was isolated by tying it in two places. When it was injected into the untied intestine, it was usually found 1 to 3 hours later in the stomach and other parts of the intestine. Only when it was injected into tied portions of the intestines was it not discovered in other parts of the gastro-intestinal tract. The author concluded that, (i) After intravenous injection of quinine, from 10.4 to 53.4 per cent of it could be found in parts of the gastro-intestinal tract in from between 15 minutes to 4 days. (ii) Only traces of quinine were discovered in the faeces.

Loibman, G. (1939) *Vlach Dyelo*, **21**, 205.

Trasentin

H. Necheles *et al* performed experiments on dogs to ascertain the effect of diphenylacetyldiethylaminoethanol hydrochloride, known as trasentin, with a view to determining (i) its toxicity, (ii) its effect on the respiratory and cardiovascular systems, (iii) its action on the hunger contractions of normal dogs, and (iv) its effect on gastro-intestinal, vesical, and gall-bladder motility in anaesthetized dogs, and also the effect on salivary secretion of the submaxillary glands. It was found that doses above 12 mg. depressed the blood pressure. Gastric hunger contractions were abolished or diminished, suggesting that the drug might be of use in cases of peptic ulcer. It was also found that trasentin diminished or abolished spasm and contraction of the stomach and intestines produced by various drugs or by vagal stimulation. Small doses of trasentin had a definitely relaxing effect on the gall-bladder, and counteracted the contracting effect of pilocarpine on the urinary bladder. Their relaxing effect on smooth musculature was considered to be due to two factors, one of which acted directly on the muscle and one on the parasympathetic nervous system.

Necheles, H., Neuwelt, F., Steiner, N., and Motel, W. G. (1939) *Amer. J. digest Dis.*, **6**, 39.

Zinc Peroxide

B. A. Johnson and F. L. Meleney investigated the antiseptic and detoxifying action of zinc peroxide on various organisms. Zinc peroxide has been successfully used in the treatment of such lesions as gas gangrene, chronic ulceration of the vagina, and pelvic abscesses. A broth suspension of the organism was incubated at 37.5 °C with zinc peroxide. The organism was said to be sensitive to its bactericidal powers if there was a marked reduction in the viable count after 4 hours and sterilization within 24 hours. Among organisms sensitive to zinc peroxide were the haemolytic streptococcus, the pneumococcus, and *Cl. welchii*. Among relatively resistant organisms were *Str. viridans* and *Staph. aureus*, *B. proteus*, *B. pyocyaneus*, and *E. coli*. The spores of *Cl. welchii* and *Cl. tetani* were also relatively resistant. The haemotoxin of *Cl. welchii* and the streptococcus were destroyed or inactivated by zinc peroxide.

Johnson, B. A., and Meleney, F. L. (1939) *Ann. Surg.*, **109**, 881.

PINEAL BODY, TUMOURS

See also Vol. IX, p. 598

Morbid Anatomy

A. F. Liber divided cavities in the pineal gland into 3 types: small cavities which cause no enlargement of the gland, cysts which are often associated with tumours such as teratoma; and cystic hydrops, which is a cyst so large that it distends the gland and may compress the brain stem or cerebellum or lead to increased intracranial tension. The author divided the symptoms produced by the latter into 2 classes, neurological and endocrine. The neurological symptoms are those of rapidly developing intracranial pressure and a case of the endocrine type has been reported in which precocious senility was thought to be due to a pineal cyst. Liber reported a case occurring in a woman of 43 in whom the signs of raised intracranial pressure were well marked. The cyst in this case contained albuminous fluid and was lined

with fibrous glia and pineal cells. It is thought that it had developed from an altered pineal diverticulum.

Primary pineal tumours often invade adjacent parts but rarely give rise to metastases. A. H. Baggenstoss and J. G. Love collected 7 cases, in 4 of which the spinal cord was involved. In a male, aged 18, who had the appearance of a 12-year-old boy and of the Lorain-Levy type of pituitary insufficiency, tentatively regarded as a tumour of the hypophysial duct, operation proved that it was a primary pineal tumour which was partially removed. After relief of headache and improvement of visual acuity, the patient began a year later to suffer from steady pain in the lumbosacral region and both thighs. Lumbar punctures between (a) the twelfth dorsal and first lumbar vertebrae, and (b) the second and third lumbar vertebrae, showed the presence of a spinal subarachnoid block. Laminectomy revealed multiple intramedullary or extramedullary tumours, some of them being discrete. Microscopically the tumours were the same as those of the original pinealoma. The cauda equina was so extensively involved that only 2 nodules were removed.

From a review of recent work on the hormones of the pineal gland Atkinson arrived at the following among his conclusions (i) As experimental pinealectomy is followed by increased growth of the comb and testes, the pineal has some influence on the gonads, by an anti-gonadotrophic hormone which inhibits the gonadotrophic hormones of the anterior pituitary (ii) A growth hormone of the pineal inhibits the growth hormone of the anterior pituitary, and there is therefore an antagonism between the 2 glands. (iii) Fat metabolism is influenced, as shown by obesity in cases of pineal tumours, and by the abeyance of the ketogenic hormone of the anterior pituitary after injection of pineal extract (iv) There is antagonism between the adrenal cortex and the pineal.

Atkinson, F. R. B. (1939) *Bull. Soc. Endocrinol., Bucarest*, **5**, 119.

Baggenstoss, A. H., and Love, J. G. (1939) *Proc. Mayo Clin.*, **14**, 72.

Liber, A. F. (1938) *J. nerv. ment. Dis.*, **89**, 782.

Clinical Picture

The association of hypogonadism, the testes showing atrophy of the seminiferous tubules and increase of the interstitial cells, with a pineal tumour which invades the brain-stem and hypothalamic region is extremely rare. In a recent case there was, as is usual in pineal tumours, internal hydrocephalus. The first symptom, somnolence, appeared 4 years before death. The history suggested that the gonads had regressed some time after the symptoms began and that the hair distribution of the normal adult male had never developed fully. The most unusual feature of hypogonadism was explained by R. A. Cleghorn *et al.* as due to disturbance, by invasion by the pineal growth, of the sympathetic tracts in the mid-brain or destruction of sympathetic centres in the hypothalamus, so interfering with the nerve supply to the pituitary which was practically normal.

Cleghorn, R. A., Hyland, H. H., Mills, J. R. F., and Imell, E. A. (1938) *Quart. J. Med.*, N.S. **7**, 183.

PINK DISEASE

See also Vol. IX, p. 603.

Treatment

Vitamin B₁

J. I. Durand *et al.* described results obtained in the treatment of 2 cases of pink disease by intramuscular injections of vitamin B₁. No previous therapy has been successful in this condition. Continuous intramuscular injections of vitamin B₁, however, in doses of 2,000 units every second day for a few weeks, gave good results; within 3 days after treatment began the patients improved, and recovery was uneventful. Attempts to give the vitamin by mouth caused relapses. Both cases were cured within 6 weeks from the beginning of treatment.

Nicotinic Acid

F. F. Tisdall *et al.* review the use of nicotinic acid in acrodynia. A comparison is drawn between acrodynia and pellagra, but, whereas pellagra has been known to respond favourably to the administration of nicotinic acid, in acrodynia nicotinic acid seems to hasten the healing of the skin lesions but to have no demonstrable

effect on the clinical course of the disease. Six infants ranging in age from 8 to 24 months were treated with nicotinic acid, in addition to the ordinary therapeutic methods, and the impression gained was that the skin lesions tended to dry up and the skin to desquamate somewhat more rapidly than in cases not receiving this treatment. The mouth lesions were unaffected.

Durand, J. I., Spickard, V. W., and Burgess, E. (1939) *J. Pediat.*, **14**, 74.
Tisdall, F. F., Drake, T. G. H., and Brown, A. (1938) *J. Pediat.*, **13**, 891.

PITUITARY GLAND DISEASES

See also Vol IX, p 611, and p 108 of this volume.

Anatomy and Physiology

Anterior Lobe Principles

J. B. Collip, dealing with the anterior pituitary, tabulated 15 physiological effects, excluding that of the chromatophore principle which is probably entirely derived from the pars intermedia. He pointed out that the number of apparently specific physiological effects of anterior lobe preparations was truly remarkable. But, in view of the fact that there are only 3 different types of cell in the anterior pituitary, it was *a priori* highly improbable that the number of individual hormonal substances elaborated by the normal functioning gland could greatly exceed the number of cell types. He had come to the tentative conclusion, as a basis for a working hypothesis, that some, if not all, of the active principles of the anterior lobe exist as prosthetic groups in a very few individual protein substances. The process of secretion from the normal intact gland could then consist in either the liberation of main protein molecules, each containing active groups of specific hormonal nature, or the liberation of the active groups themselves from mother molecules by enzymatic or other action. He divided the long list of physiological effects which could be elicited by anterior lobe extracts into 2 groups: (i) those due to trophic influences of the extracts upon outlying glands, such as thyrotrophic, gonadotrophic, and adrenotrophic, and (ii) those that appear to be more or less direct effects of some constituents of the extract acting in the periphery.

The Growth Hormone

J. Freud *et al* in their report of an experimental research involving complete hypophysectomy in a large number of rats, discussed the question of the existence of a special and single growth hormone in the anterior pituitary. In spite of the strong evidence that hypophysectomy causes dwarfism and that injection of alkaline extracts of the pituitary is followed by gigantism (Evans and Long, 1921), doubt has been thrown on the existence of a growth hormone. Thus O. Riddle and R. W. Bates (1938) suggested that some pituitary extracts owe their action upon growth to a 'balanced combination' of prolactin, thyro-, or perhaps adreno-trophic hormones, rather than to a special growth hormone. Freud and his colleagues cannot definitely say whether or not the growth-promoting effect is due to one substance, but they state that their highly purified preparations were 'practically free' from prolactin, cortico-, or thyro-trophic activity. As the result of complete hypophysectomies in 70 rats and a dummy operation in which the epispheoidal dura mater was opened and the anterior pituitary damaged but not removed in 30 control rats, it was found that after hypophysectomy longitudinal growth of bone ceases, best shown in the tail by measurement and X-ray examination, and that the epiphyses soon become closed, and that when union has taken place the process cannot be reversed by treatment with growth hormone. But, if this treatment is begun immediately after removal of the pituitary, the epiphyses are not closed and normal longitudinal growth in the tail continues. The defect in growth due to hypophysectomy is definitely localized in the growing epiphysal cartilage. There was not any change in the bone tissue, and desmal bones, such as those of the cranium, develop normally. As growth hormone has a biologically typical point of attack at the proliferating cartilage, the terms 'growth hormone' and 'chondrotrophic hormone' are synonymous.

Specific Metabolic Stimulant in Anterior Pituitary

A specific metabolic stimulant, other than the thyrotrophic hormone, in pituitary extracts has been reported by D. K. O'Donovan and J. B. Collip. It raises the oxygen

consumption with a corresponding fall in the respiratory quotient a few hours after it has been injected, and also decreases nitrogen metabolism. Experiments were made on rabbits with an extract prepared from the pituitaries of the ox, sheep, and pig. The active principle was present in both anterior and posterior lobes, but in the highest concentration in pituitary colloid and in extracts of the pars intermedia. It is thermostable, resistant to alkali and pepsin, destroyed by trypsin, and adsorbed by charcoal. In these characters it exactly resembles the melanophore-expanding hormone of the pars intermedia.

Anterior Pituitary Control of Urinary Excretion

In a discussion on the relation of the anterior pituitary to the control of urinary excretion, B. G. Shapiro argued that the results of large doses of oestrin and of anterior lobe preparations provided evidence that the anterior pituitary in man exerted a diuretic effect. If the anterior lobe was inhibited by large doses of oestrin in diabetes insipidus, there was a decrease in the urinary output. If subsequently anterior pituitary was given the urinary output increased. It was suggested that the polyuria of Cushing's syndrome might be due to hyperactivity of the anterior lobe rather than to pressure of the tumour on the posterior lobe, because often there was not any tumour, but simply a hyaline change in the basophil cells. A tumour if present was always very small and situated in the anterior part of the anterior lobe, and could not press on the posterior lobe.

Collip, J. B. (1938) *Edinb. med. J.*, 4th ser., **45**, 782.

Evans, H. M., and Long, J. A. (1921) *Anat. Rec.*, **21**, 61.

Ireud, J., Levie, L. H., and Kroon, D. B. (1939) *J. Endocrinol., Lond.*, **1**, 56.

O'Donovan, D. K., and Collip, J. B. (1938) *Endocrinology*, **23**, 718.

Riddle, O., and Bates, R. W. (1938) *J. biol. Chem.*, **123**, 5.

Shapiro, B. G. (1938) *Lancet*, **2**, 1457.

Hypopituitarism

Acute Pituitary Insufficiency

After appendectomy—E. Seeger published a case of acute pituitary insufficiency which led to death after an operation for the removal of the appendix. The patient progressed badly after the appendectomy, which was quite simple and uncomplicated. All attempts to improve her condition failed and she died for no obvious reason. Necropsy revealed an atrophic pituitary gland. By questioning the relatives it was found that she had had temporary amenorrhoea for 30 years. A few days before the operation her skin became more parched and her hair fell out. It appears that the balance established for 30 years was disturbed by a simple short operation, leading to death of the patient.

Treatment

Thyrotrophic hormone—A. W. Spence and I. J. Witts reported observations on two men, aged 50 and 20, who had been operated upon for a chromophobe adenoma and a suprasellar cyst, and were given for a prolonged period pituitary thyrotrophic hormone to obviate the effect of hypopituitarism. As in experimental animals (Anderson and Collip), the administration of thyrotrophic hormone was followed by a rise in the basal metabolic rate for a time, and then by a fall to the previous low level in spite of continued treatment. The blood serum of one patient inhibited the action of thyrotrophic extract injected into guinea-pigs. In both patients the basal metabolic rate rose after the subsequent administration of thyroid extract, but large doses were necessary. In general the effects of the substitution treatment were disappointing, and it was suggested that, when employed, it should be limited to 3 weeks with alternating periods of rest. In one patient severe cramps disappeared after the thyrotrophic hormone was given, and the same patient, previously achlorhydric and showing atrophy of the gastric mucosa gastroscopically, became possessed of hydrochloric acid in the gastric juice and gastric mucosa showing, through the gastroscope, signs of regeneration. The speculative question of anterior pituitary control of the gastric mucosa was raised.

Anderson, E. M., and Collip, J. B. (1934) *Lancet*, **1**, 784.

Seeger, E. (1939) *Munch. med. Wschr.*, **86**, 882.

Spence, A. W., and Witts, I. J. (1939) *Quart. J. Med.*, N.S. **8**, 69.

Tumours

Diagnosis

Cossa *et al.* reported that, in 6 cases with an enlarged anterior lobe of the pituitary the curve of provoked hyperglycaemia, which was abnormal before treatment, became normal after radiotherapy. Improvement of the curves was parallel with the functional modification produced by radiotherapy in the anterior lobe of the pituitary. The curve was different in the different types of adenoma. (i) In acidophil adenoma the curve went higher than in a normal case, and reached its highest point quickly in half an hour; descent took two or two and a half hours. (ii) In basophil adenoma the ascent was also rapid, went up still higher, and remained so for some time, it fell more rapidly than in acidophil adenoma. (iii) In chromophobe adenoma 2 different types of curve were observed, one very low, and the other corresponding to the high normal type. The first was observed in cases of cachexia, the other in dystrophia adiposo-genitalis. The number of cases examined in this way was fairly small.

Treatment

Surgical—Dealing with the relief of symptoms and signs due to pressure on the optic chiasma or the diencephalon by a pituitary adenoma, G. Phillips recommended the trans-sphenoidal route of approach when the tumour was certainly intrasellar. The main risk of this procedure was an ascending infection during the period of cerebrospinal rhinorrhoea. Meningitis was rare when the operation was carried out between the flaps of mucous membrane on either side of the nasal septum.

Cossa, Augier, and Rivoire (1939) *Rev. neurol.*, **71**, 267.

Phillips, G. (1938) *Brit. J. Surg.*, **26**, 242.

Cushing's Syndrome

Aetiology

F. Anderson and W. Haymaker found that extracts of the blood and urine of patients with Cushing's syndrome (pituitary basophilism) contained an excessive amount of a substance which resembled adrenal cortical hormone in its power of prolonging the life of adrenalectomized rats. These observations add further support to the hypothesis that Cushing's syndrome is due to an over-production of the adrenal cortical hormone.

Morbid Anatomy

G. Hall *et al.* reported a case of Cushing's syndrome (pituitary basophilism) in a man, aged 26, without any endocrine tumour. Death was immediately due to toxæmia from gangrenous cellulitis. At the necropsy the anterior pituitary did not contain a definite basophil adenoma; there was an area of dilated sinusoids, and close to this was a small collection of basophil cells which A. C. Crooke in 1935 reported to show the hyaline change characteristic of the syndrome. The pars intermedia showed several tubular spaces containing colloid, one of which was dilated to form a cyst visible to the naked eye. The adrenals were free from cortical adenomas and hyperplasia. The suggestion was made that those endocrine diseases more often seen in females, such as toxic goitre, the adreno-genital syndrome, and Cushing's syndrome, might be an expression of the increased complexity of the cyclical changes in women associated with menstruation and pregnancy.

Clinical Picture

F. Evelyn Anderson *et al.*, discussing hormone and electrolyte studies of patients with the hyperadrenocortical syndrome (Cushing's syndrome), supplemented the observations of Anderson and Haymaker by a report on the urinary excretion of sodium and potassium and the blood level of these in 3 patients with Cushing's syndrome. They compared these findings with those in Addison's disease. The plasma electrolytic pattern in Cushing's syndrome and in Addison's disease are diametrically the opposite. It was argued that patients with Cushing's syndrome should be benefited by a low sodium and a high potassium intake. This form of treatment proved effective in one case, the blood pressure and weight being reduced, and headache and generalized pain being relieved.

Diagnosis

A. C. Crooke and R. K. Callow, in an article on the differential diagnosis of forms of basophilism (Cushing's syndrome), particularly by the estimation of urinary

androgens, reported in detail 4 cases, in 2 of which there was a primary carcinoma of the adrenal cortex, an adrenal tumour being palpable in one, and in the other shown by X-rays with Cahill's method of bilateral insufflation of air into the perirenal tissues, and confirmed by necropsy in one case and by operation in the other. These 2 cases are those elsewhere described as the adreno-genital syndrome of adrenal virilism in which, as in Cushing's cases, hyaline change in the basophil cells of the anterior pituitary has been found by Crooke (1935). In the two other cases there was not any adrenal tumour, the condition originally described by Cushing (1932). Apart from demonstration of the presence of an adrenal tumour, a differential diagnosis is difficult, and the authors of this paper say that it has been unreliable by ordinary clinical examination. As removal of an adrenal tumour is most important, a further means of predicting its presence is highly desirable. Examination of the urine for the amount of androgens showed that in the 2 patients with adrenal tumours there were high values in the calorimetric assay of 17-ketosteroids or in the biological assay of androgens; this increase of 17-ketosteroids was largely due to *trans*-dehydroandrosterone which was isolated from the urine in amounts many times as great as those in normal men and women. The other 2 cases, without adrenal tumours, gave low values by comparison in the calorimetric or biological assay, and thus this test should be helpful in the differential diagnosis between basophilia with adrenal tumours and basophilia without adrenal growths.

Anderson, L., and Haymaker, W. (1938) *Proc. Soc. exp. Biol., N.Y.*, **38**, 610.

— and Joseph, M. (1938) *Endocrinology*, **23**, 398.

Cahill, G. F. (1935) *J. Urol.*, **34**, 238.

Crooke, A. C. (1935) *J. Path. Bact.*, **41**, 339.

— and Callow, R. K. (1939) *Quart. J. Med., N.S.*, **8**, 233.

Cushing, H. (1932) *Johns Hopk. Hosp. Bull.*, **50**, 137.

Hall, G., Kellett, C. F., and Stephenson, G. I. (1939) *Lancet*, **1**, 862.

PLAGUE

See also Vol. IX, p. 675, and p. 148 of this volume.

Treatment

M & B 693

H. Schutze tested the efficacy of M & B 693, soluseptasine, and a diaminodiphenylsulphone glucoside (sulphone) against infection with *B. pestis* in rats and mice, the drug being given with food and drink and by subcutaneous injection. M & B 693 was the most effective drug against plague in both rats and mice, whereas soluseptasine protected rats but not mice, and sulphone mice but not rats. Anti-plague serum injected subcutaneously at the same time as the test dose of *B. pestis* produced results comparable with those of M & B 693.

Schutze, H. (1939) *Lancet*, **1**, 266.

PNEUMONIA, LOBAR

See also Vol. IX, p. 713, and Cumulative Supplement, Key No. 1279.

Aetiology and Bacteriology

It has been known for some time that pneumococci occur in the dust of rooms in which pneumonic patients have been treated and in the mouths of healthy carriers, and are of the same type in members of the same household. But whether dust is continually reinfected by healthy carriers or was originally infected by the pneumonic patient and was responsible for the carriers is not settled. According to E. G. Stillman, in order to answer this question it is necessary to discover how long pneumococci remain viable in dried sputum under conditions resembling those of nature. He found that the pneumococci survived for months if exposed to diffused daylight, and that if they were stored in the cold they lived 4 or 5 times longer. This is of interest since pneumonia is a disease of the winter months. Stillman discussed

the method of transference and carriage of pneumococci; it is possible that the carrier may have a focus of infection in the accessory nasal sinuses from which the organism is transferred to the nose and throat. Pneumococci Types I and II, which are usually associated with lobar pneumonia, are rarely carried by normal individuals. Webster has found that individuals vary in their ability to carry the pneumococcus, some being always free and some transient, some periodic, and some chronic carriers.

Stillman, F. G. (1938) *J. infect. Dis.*, **63**, 340.

Complications

Gastric and Renal Lesions

R. Opsahl described a very rare but apparently typical complication of pneumonia which manifested itself by haematemesis on the eighth day of the disease, followed by uraemic coma which terminated in death 2 days later. The necropsy revealed an acute interstitial nephritis and multiple ulcers in the stomach. This condition was first described by Dieulafoy in 1899 as *gastrite ulcéreuse pneumococcique*. There were only 11 cases previous to the publication of the author's case, though it is assumed that the condition occurs more frequently but remains undiagnosed.

Opsahl, R. (1939) *Acta med. scand.*, **100**, 318.

Treatment

Sulphonamide Drugs

An investigation carried out in the native hospital, Nairobi, on 100 natives with pneumonia admitted between August and November 1938, is reported by I. I. Anderson and R. M. Dowdeswell. Of these 50 were treated with M & B 693 (sulphapyridine) and the remainder were given the customary non-specific treatment. Those patients dying within 24 hours of admission, and those who had been ill for more than 5 days before admission were not included in the selection. The dosage employed was 2 half-gram tablets every 4 hours with an initial dose of 4 tablets (2 g.). The dosage was reduced for children according to age. Administration was continued for 24 hours after the temperature had fallen to normal except in a few cases in which there was a slight rise of temperature in the second week. The largest total quantity given to a single patient was 40 g., the average being 18.5 g. There were 8 deaths in the control series compared with one in those treated by M & B 693, whereas, in many cases in the control group, the temperature first reached normal at the crisis, in the treated group the temperature first fell to normal within 24 hours of the commencement of treatment in 26 cases, and within 48 hours in 44. In every case the temperature reached normal in 3 days. In this small series it was impossible to correlate clinical findings with different pneumococcal types, but the drug appeared to be active against all types.

N. Plummer and H. Insworth published the results of sulphapyridine treatment in 88 cases of lobar pneumonia in the Bellevue Hospital, New York. The dose of the drug, always given by the mouth, was usually 2 g. (30 gr.) for the initial dose followed by 1 g. every 4 hours until the desired therapeutic effect was obtained, the average total amount taken was 16 g. but one patient received 46 g. Of the 88 patients, 7, or 8 per cent, died as compared with an expected mortality of 25 to 35 per cent. Among the 24 cases of Type III pneumococcus the percentage was 8. (A footnote, added just before publication, stated that 157 cases of pneumonia had been treated with a mortality of 15, or 9.5 per cent, of 36 cases of Type III pneumonia 2 proved fatal, or 5.6 per cent.) The clinical response to the drug was as remarkable as the reduction in the mortality-rate. In 45 of the 88 patients the temperature dropped to normal in 24 to 36 hours, the active phase of the disease was considerably shortened, though the signs of consolidation seemed to run through the usual course. There was not any fall in the leucocyte count, but in several cases with an initial leucopenia the count became normal after the treatment was started. In 20 of the 88 cases both the drug and specific anti-pneumococcal serum were given without any death. (In the later total of 157 cases 40 were given both the drug and the serum with 2 deaths or 5.6 per cent.) The chief unfavourable effects were nausea (55 per cent of the 88 cases) and vomiting (40 per cent), and in 10 per cent these symptoms were so severe as to make it advisable to discontinue the drug. There was absence of toxic hepatitis, nephritis, neuritis, and agranulocytosis.

J. C. Meakins and F. R. Hanson treated 30 patients with pneumonia by M & B 693

with one death, or 3 per cent (a man aged 87 with a recent left bundle-branch lesion). The usual dose of the drug was 2 g. repeated in 4 hours, and then 1 g. every 4 hours until the temperature had remained normal for 48 hours, and then 1 g. every 6 hours for 24 hours; the average total dose was 27 g. The attempt was made to find some correlation between the amount of the drug taken and its concentration in the blood. After 4 or 5 g. had been given the concentration varied from 3.6 to 14.2 mg. per 100 c.cm. and variation occurred in the same patient. In general the dosage given produced a concentration in the blood of between 5 and 10 mg. per 100 c.cm. in the first 12 to 18 hours, and this was maintained by 1 g. every 4 hours. Vomiting once or more often occurred in 20 of the 30 cases and in 3 instances necessitated discontinuance of the drug. It was hoped that the soluble sodium salt, which could be given rectally or intravenously, would correct this. There was not any leucopenia or evidence of agranulocytosis.

E. K. Marshall and P. H. Long gave intravenous injections of 5 per cent sodium sulphapyridine to 30 patients, as it was found that its absorption from the gastrointestinal tract was at times somewhat uncertain. In pneumococcal pneumonia, when the patient was moderately ill, oral administration of 4 g. in the first dose was followed by 1 g. 4-hourly until the patient's temperature had been normal for 48 hours. The dose was then reduced to 1 g. 6-hourly and was continued later as 0.5 g. until all pulmonary signs had cleared. In severe cases, 0.05 g. of sodium sulphapyridine per kilo of body weight was injected in a 5 per cent solution in sterile distilled water at the rate of 5 c.cm. per minute. This may be repeated at intervals of 6 to 8 hours, care being taken not to push the needle through the wall of the vein, otherwise sloughing results. If 1 g. of sulphapyridine is being given orally every 4 hours, usually 2 injections will suffice. The authors are of opinion that a blood level of 4 mg. per 100 c.cm. is desirable in the pneumonia of adults to render the drug effective.

D. Graham *et al.* conducted a series of experiments in cases of pneumococcal pneumonia, using the first group as controls, treating another with specific rabbit serum, and the third with M & B 693. The mortality-rates were 23 per cent, 12 per cent, and 6 per cent respectively. M & B 693 was particularly successful in cases with bacteraemia, the mortality-rate in these cases being 17 per cent, as compared with 50 per cent in the control group and 57 per cent in the serum-treated group. The average total dosage of M & B 693 administered was approximately 39 g., large doses being given in the first 48 hours of treatment. All cases showed a marked decrease in temperature within 36 hours of the commencement of treatment. Differentiation between extension of the pneumonic process and drug fever may be made by determining the white cell count. Where the effect of the drug is responsible for the rise in temperature, there is no increase in the white cell count. In these cases, cessation of the drug results in a return of the temperature to normal.

A. T. Wilson *et al.* treated a group of 35 children suffering from pneumonia with sulphapyridine (M & B 693). Another group of 35 children equivalent in age, and presenting a similar clinical picture before admission to hospital, was kept as a control. In the sulphapyridine group, on an average, clinical improvement occurred and was maintained from the fourth evening after commencement of the pneumonia. The temperature fell on the fifth day and by the eighth the patient was considered to have recovered. As compared with this, the control group, on the average, showed improvement on the seventh day from the onset, the temperature fell significantly early on the ninth day, and recovery was established by the twelfth. Although marked variations occurred in the blood levels it was concluded that a concentration of approximately 4 mg. of the drug per 100 c.cm. of blood induced a satisfactory response. The dosage was calculated at the rate of 1 grain to 1½ grains per pound of body weight in each 24 hours. The toxic effects observed in this group were insignificant, only 2 cases developing skin reactions. All patients in both groups recovered.

Sulphonamide Drugs and Serum

I. H. Maclean *et al.* found that the enormous variation in the sensitivity of pneumococci to M & B 693 was not associated with the type of pneumococcus but with the strain, and described a method of testing *in vitro* the sensitivity of a strain to the drug. If the infecting organism was very sensitive, treatment with the drug would probably be effective; if it was only moderately sensitive, it was very likely that some increase in immunity would be necessary in addition to M & B 693 treatment; if the organism was insensitive to M & B 693 in concentrations attainable

in the human body there was not any justification for embarking on a course of M & B 693 treatment, which could not do good and might have serious toxic effects. A single dose of pneumococcal vaccine given to mice or rabbits profoundly affected the course of an experimental infection in those animals when treated with M & B 693. The combined utilization of vaccines and M & B 693 in all cases of pneumonia in man was therefore suggested. On experimental evidence pneumococci could, in an infected animal treated with M & B 693, establish a tolerance or fastness to the drug. This made it essential that initial doses should be large and that the immunity of the body should be raised to as high a level as possible by any means (active or passive, specific or non-specific).

M. Finland and J. W. Brown carried out a series of studies to ascertain the effect of sulphanilamide and serum, alone and in combination, on the growth of Type III pneumococci in pneumonia. It was found that sulphanilamide in concentrations of about 7 mg. or more per cent exerted a bacteriostatic action on large numbers of Type III pneumococci in the blood of non-pneumonic individuals or of patients ill with pneumonia caused by this organism. The drug probably does not influence phagocytosis in this type of blood. It usually exerts no bactericidal effect in a concentration of 10 mg. per cent but may do so occasionally with higher concentrations. Therapeutic Type III anti-pneumococcal rabbit's serum induces anti-pneumococcal activity in the blood of patients who contract this type of pneumonia. The combination of antiserum and sulphanilamide produces a greater bacteriostatic and bactericidal effect than an equivalent amount of either given separately. The general mortality in a series of 56 cases treated by this therapy remained as high as 43 per cent. The duration of the disease was actually greater in patients treated with serum or sulphanilamide than in the untreated group. The authors consider, however, that the general effect of such treatment in individual cases suggests that this combination is an effective means of countering pneumococcus Type III pneumonia.

M. Finland *et al.* also investigated the combined use of sulphonamide drugs and a serum, a group of 95 patients showing specific types of pneumococci were treated with sulphapyridine; a second group of 80 patients received sulphapyridine and specific serum, a third group of 167 patients were treated with specific serum only. In the third group the bacteraemia incidence averaged 27 per cent, the majority of cases being in the older age group, and the death-rate was 13 per cent. In the group treated with sulphapyridine alone the death-rate was 15 per cent, although the incidence of bacteraemia was only 17 per cent. In the group of 80 patients in which the combined serum and chemotherapeutic treatment was used, the total bacteraemic incidence was 50 per cent. The mortality-rate was 22 per cent, which was regarded as distinctly favourable in view of the fact that in similar cases receiving neither specific serum nor drugs, the death-rate might have been expected to be as great as 75 to 90 per cent, and where specific serum alone was used, 50 to 60 per cent. An interesting observation made was that Type III pneumonia responded well to chemotherapeutic treatment. In this series only two Type III bacteraemia cases recovered and these were treated with sulphapyridine alone, while in an earlier series Type III cases were found to respond to sulphanilamide. The specific antibodies produced in both rabbits and horses for this type are of low potency and the additional use of sulphanilamide or sulphapyridine was of considerable value. It was found in the majority that when serum alone was used symptoms abated in from 6 to 24 hours. When a combination of serum and sulphapyridine was used, it was found that the drug could be omitted within 12 to 36 hours of the first dose, and smaller doses of serum were necessary than when the drug was not used. When sulphapyridine was used alone symptoms were more prolonged and it was found that the drug must be given for a minimum of 48 to 72 hours after the temperature had fallen. Apart from impaired renal function which occurred in 2 cases, but which could not definitely be related to the drug, no untoward symptoms other than those usually associated with this type of drug were observed.

In all cases of pneumonia the authors advise the taking of a blood culture before treatment commences. The institution of sulphapyridine therapy as soon as diagnosis is made, combined with the administration of specific serum at the earliest possible moment, is the treatment of election.

Serum Therapy

B. Horn studied a series of 245 cases of lobar pneumonia. From the results obtained with specific serum, he concluded that, if sufficient is given within the first 4 days, it is possible in the majority of cases to curtail the course of the disease and to effect

an earlier recovery than would otherwise have taken place. The effectiveness of serum therapy is enhanced if it is administered early in the course of the disease, but at whatever stage the patient is seen the author advised the injection of Type I serum immediately and in large amounts. Other types, for which specific serum is advisable, should be treated similarly. Stress is laid on the importance of correct typing of the pneumococcal strains. In Type I the mortality-rate was reduced from 10 to 3.6 per cent and in Types V, VII, VIII, and XIV from 12.5 to 3 per cent. Serum sickness was observed only in 5 per cent of cases. In the group of cases under review the rate of mortality was considerably lessened and serum sickness was only observed in a small percentage of cases. Skin and eye tests for sensitivity should be performed.

N. Plummer investigated the results of the serum treatment of pneumonia, other than those of Types I and II. The higher types account for over 50 per cent of all pneumococcal pneumonia. In the very fatal Type III pneumonia, 6 out of 9 patients treated with concentrated rabbit serum recovered. In 111 cases of Types IV, V, VII, VIII, and XIV, the clinical response to serum treatment was good and the mortality-rate was lessened. The author found that the refined preparations of concentrated horse and rabbit serum produced very few serum reactions.

Serum Dosage by Skin Tests

The value of skin tests with specific polysaccharides in controlling serum dosage in pneumococcal pneumonia is stressed by C. M. MacLeod *et al.* and the methods used for obtaining the tests are described. The results apply not only to Types I and II but also in disease caused by pneumococcus Types III, V, VII, and VIII. In a series of 104 patients, the skin test was of value in the treatment of 77 per cent. In cases in which a positive reaction was shown before the administration of specific antiserum, and when the disease was still advancing, its value as a control agent was nil. This occurred in 12.5 per cent of cases under review. From results in patients who yielded a negative reaction before serum therapy, the greatest value of the test was found to be where a specific action of the immune serum was rendered effective by adequate cellular response on the part of the patient. In these the development of a positive test serves to show the optimal amount of serum to be given. A specially important need when performing these skin tests is the purity of the preparations of specific polysaccharides used.

Hydroxyethylapocupreine

W. W. G. MacLachlan *et al.* treated a number of cases of pneumococcal pneumonia with hydroxyethylapocupreine. It was given orally in doses of 15 gr., every 3 hours, day and night for 3 to 5 days. Sometimes this treatment produced nausea and vomiting. The monohydrochloride was given intravenously in a 2 per cent solution, 50 c.c.m. (containing 15 gr.) being given in from 7 to 10 minutes every 3 hours. Thrombosis of the veins of the arm at the point of injection occurred in some cases but in no case were any visual symptoms produced. The mortality of pneumococcal pneumonia was greatly reduced, and figures obtained were identical with those of a serum-treated series of patients suffering from the same type of pneumonia. In mixed infections the results were found to be not so good.

Oxygen

More frequent use of oxygen is advocated by F. B. Davies. In a series of 152 consecutive emergency calls for oxygen the predominant condition was, as would be expected, pneumonia, but other cases treated included acute coronary occlusion, myocardial failure, uraemia, septicaemia, and carbon monoxide poisoning. Stressing the importance of the early use of oxygen, the author found that in a group of 77 patients to whom oxygen was administered on the first day the mortality-rate was 3.8 per cent, but in another group of 47 in which oxygen therapy was delayed till the fifth day, the mortality-rate was 63.8 per cent. Administration of oxygen, apart from that by inhalation apparatus, may be by one of 3 kinds of tent: the motor-driven, the convection, and the 'open top', the latter being particularly useful in the case of children and infants. During treatment an adequate concentration of oxygen must be maintained and the removal from an oxygen tent should be performed gradually.

Artificial Pneumothorax

F. G. Blake treated 72 patients suffering from lobar pneumonia with artificial pneumothorax and concluded that, although it relieved the pain of associated pleurisy, it had no specifically beneficial effect upon the pneumonia. It is unsuitable

treatment in cases of more than 72 hours' duration and in those in which adhesions have formed, as these prevent the collapse of the lung.

- Anderson, T. F., and Dowdeswell, R. M. (1939) *Lancet*, **1**, 252
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 Horn, B. (1939) *Ann. intern Med.*, **12**, 922.
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 Marshall, E. K., and Long, P. H. (1939) *J Amer med Ass.*, **112**, 1671
 Meakins, J. C., and Hanson, F. R. (1939) *Canad med Ass J.*, **40**, 333
 Plummer, N. (1938) *J. Amer med Ass.*, **111**, 694
 — and Ensworth, H. (1939) *Bull N.Y. Acad Med*, 2nd ser., **15**, 141
 Wilson, A. T., Spreen, A. H., Cooper, M. L., Stevenson, F. E., Cullen, G. E., and Mitchell, A. G. (1939) *J. Amer. med Ass.*, **112**, 1435

PNEUMOTHORAX, SPONTANEOUS

See also Vol. IX, p. 743, and Cumulative Supplement, Key No. 1280

Tense or Valvular Pneumothorax

Treatment

Injection of poppy seed oil—H. Hennell and M. F. Steinberg treated 5 patients (in another the treatment was not completed) with a tense pneumothorax, in which a pleuro-pulmonary communication acts as a one-way valve allowing air to enter the pleural cavity with inspiration but not to escape with expiration, by the production of a chemical pleurisy set up by injection into the pleural cavity of iodized poppy seed oil or by a saturated solution of dextrose (67 per cent). The pleurisy led to closure of the pleuro-pulmonary communication and the 5 patients were clinically cured. It was often necessary to repeat the injections, and in the 6th patient both dextrose and iodized poppy seed oil were used without effect before he left the hospital against advice. Valvular pneumothorax was not common, but caused distressing symptoms. Usually due to acute lung disease, in some instances the aetiology was obscure, so-called 'idiopathic' tense pneumothorax. In the majority of cases a spontaneous cure occurred; when sufficient air had entered the pleural cavity the lung collapsed and the communication closed; the air in the cavity acting as an irritant, the pneumothorax was then absorbed and the lung expanded again. But in some cases the valvular pneumothorax lasted for months or years, and these were suitable for this treatment by the production of chemical pleurisy. From a review of the reported cases it appeared that so far 12 patients had received this form of treatment. After injection of the dextrose or oil the patient must rest in bed on the affected side for a long time, sedatives must be given, and all respiratory effort, such as coughing, should be suppressed, and no attempt should be made to aspirate the air.

Hennell, H., and Steinberg, M. F. (1939) *Arch intern Med.*, **63**, 648

POLIOMYELITIS AND POLIOENCEPHALITIS

See also Vol. X, p. 12, and p. 42 of this volume.

Aetiology

M. Stillerman and A. E. Fischer reported 13 cases of acute poliomyelitis following removal of tonsils and adenoids, 9 being of the bulbo-encephalitic type. The interval

of 10 to 22 days between the operation and the incidence of bulbo-encephalitis suggested that the virus entered the nervous system through the area of the operation; for the virus travels along nerve-trunks and the nerves of the tonsillar and pharyngeal walls lead to the brain-stem. It was suggested that tonsillectomy and adenoidectomy should not be undertaken when poliomyelitis is epidemic.

As cholesterol inactivates the virus of poliomyelitis either by adsorption or destruction, and as ergosterol has the same hydrocarbon filament as cholesterol, J. A. Toomey and W. S. Takacs investigated the action of ergosterol on poliomyelitis virus. Animal experiments showed that ergosterol and crystalline vitamin D exerted an inhibitory effect on suspensions of the purified virus but, like cholesterol, did not inactivate unpurified poliomyelitis virus.

Stillerman, M., and Fischer, A. E. (1938) *Amer. J. Dis. Child.*, **56**, 778

Toomey, J. A., and Takacs, W. S. (1938) *Amer. J. Dis. Child.*, **56**, 1274

Clinical Picture

Mostyn L. Powell, reviewing the symptomatology of acute poliomyelitis as manifested by 488 cases in a recent epidemic in Melbourne, finds 6 clinical groups. Group I is largely hypothetical, representing a mild undiagnosable attack with a mere suggestion of a pyrexial state and conferring a lasting immunity. A mild febrile phase, perhaps unrecognized, occurred in Group II followed by a very mild paralysis. Serological immunity also results in this group. Group III represents abortive poliomyelitis. The febrile stage is mild and there are no spinal signs, cervical stiffness, or resulting paresis. Group IV is Draper's 'diomedary' type in which there are two febrile spells, at an interval of 2 or 3 days during which the child is apparently quite well. The second wave, which is always of greater intensity than the first, is accompanied by the onset of paralysis. The fifth group represents the ordinary acute type in which the febrile stage is followed by the paralytic stage. Group VI is called non-paralytic poliomyelitis. The febrile phase is acute and all signs and symptoms of the condition are present except that at no time is there any paralysis. Cells are present in the cerebrospinal fluid and, as in Groups I and III, the condition is probably caused by a dosage or virulence of the virus not quite equal to the patient's power of resistance. Fever was present in all these cases.

Powell, M. L. (1938) *Med. J. Aust.*, **2**, 276.

Diagnosis and Differential Diagnosis

M. L. Powell regarded lumbar puncture as confirmatory evidence rather than an aid to definite diagnosis in most cases. At least 90 per cent of cases were diagnosable without it. The fluid is often normal in the early cases when lumbar puncture would be of most use and the changes in the fluid, such as the lymphocytosis, occur in other conditions. Lumbar puncture was of most use in cases which, although bearing some resemblance to poliomyelitis, were regarded as being some other condition, e.g. spontaneous subarachnoid haemorrhage.

F. O. MacCallum and G. M. Findlay described a case of lymphocytic choriomeningitis which had the clinical appearance of acute poliomyelitis and was first diagnosed as such. The virus of lymphocytic choriomeningitis was once isolated from the cerebrospinal fluid and twice from nasopharyngeal washings. The virus was still present in the nasopharynx 8 and 12 weeks after the onset though after the eighth week its presence in the cerebrospinal fluid could not be demonstrated. On discharge the patient still had paralysis of the legs, but muscular power had returned in other regions. No specific antibodies to the virus were produced by the patient.

MacCallum, F. O., and Findlay, G. M. (1939) *Lancet*, **1**, 1370

Powell, M. L. (1938) *Med. J. Aust.*, **2**, 276.

Treatment

Prophylaxis

Zinc sulphate.—The control of poliomyelitis by chemo-prophylaxis applied to the olfactory region is suggested by E. W. Schultz (1938, a) in the form of a postural method of application of a 1 per cent solution of zinc sulphate. The subject is put on a table with the head in the fully inverted position. A maximum of 0.5 c.cm. of fluid is then introduced slowly, with a medicine dropper, into each nasal space. After the

required amount has been inserted the patient is kept in the inverted position for one minute, then turned over to the prone position and instructed to lift his head and sniff outwardly to discharge any excess fluid. It is essential that the solution should come into contact with the entire olfactory area. Complete anosmia is produced, which is more lasting in adults than in children. It may persist for months and it is suggested that its continued presence may indicate the interval of time which should elapse between treatments, if adequate protection is to be ensured. Apart from the anosmia the only reaction is a severe headache which may last for 3 to 6 hours after treatment. The need for further experiments to ascertain the most effective prophylactic agent in man is stressed.

Schultz (1938, b) points out that, although the protective action of zinc sulphate solution in prevention of experimental poliomyelitis has been determined in monkeys, it is not possible to state that the same prophylactic measures hold good in man. It is not definitely established that, in man, the infection enters solely by way of the olfactory nerve, and in addition it is not known how far the risk of inducing a permanent anosmia by the administration of zinc sulphate may be eliminated without sacrificing the effectiveness of the measure. Lasting anosmias, following the application of zinc sulphate, have occurred only in adults, children having regained their sense of smell within 2 weeks. Adults tend to suffer more severe post-treatment reactions than children. The postural method of administration adopted by Shahinian consists of completely inverting the head and running into the olfactory sulcus small quantities of the solution (0.5 c.c. in drops). This flows along the nasal groove and fills the meatus to a height which immerses the olfactory area. The author suggests that the drug should be washed out from the nasal chamber by physiological saline shortly after its application.

Following upon prophylactic treatment against poliomyelitis by means of the zinc sulphate nasal spray, F. F. Tisdall *et al.* found that persistent anosmia was more prevalent among adults than in children. A group of 4,713 children between the ages of 3 and 10 received two sprayings (at clinics) at an interval of 10 to 12 days and a second group of 520 children received one spraying (at clinics). Very few, if any, of these children reported any lasting anosmia. In private practice it was assumed that a number not exceeding 5,000 received sprayings and of these 52 at the end of six months had reported persisting disturbances of smell, combined in some cases with disturbances of taste. Only one was a child under 10 years. The author suggests that a careful study of the effect of zinc sulphate on the mucous membrane of human beings is essential to determine whether the olfactory area is damaged by its application.

R. F. Ashley, reviewing the effect of chemicals on the nasal mucosa of humans, their methods of application, and the prophylactic results obtained, stated that with the use of zinc sulphate the sense of smell always returns. Since the success of the treatment depends upon the thoroughness of nerve-blocking, Ashley suggested that the return of the sense of smell should be an indication for further application of the chemical. Children up to 10 years require 0.5 c.c. of fluid, children between 10 and 14 years 0.4 c.c., and adults 0.25 c.c. So far this method of prophylaxis has failed to give protection during epidemics, but many of the methods of application were faulty and further tests are required. In any case, the period of protection is short and no immunity to the virus is given to the individual. However, at present it is the only method which gives any chance of protection from the disease.

Of the Infection

Pettit's serum.—While agreeing that convalescent serum is not of any use in the treatment of acute poliomyelitis because, in more than a third of such convalescents, there is not any evidence of antibodies in their serum, A. Casassa strongly recommended the antipoliomyelitic serum of Pettit (serum S A P) obtained from horses or chimpanzees, which contains antibodies. He has used it for years and found that its use is followed by a cure, even when paralysis has been present for 10 or 12 days not only in children but in adults; it also prevents the extension of poliomyelitis from the spinal cord to the medulla, and has reduced the mortality.

Of Paralysis

Underwater exercises.—K. G. Hanson describes his method of underwater exercises following poliomyelitis. He considers that rest in plaster and support of the affected muscles are of prime importance, associated with carefully graded re-education of the muscles at a later date. Meanwhile the tone of the muscles is maintained by heat

and gentle massage. The circulatory disturbance the author believes to be secondary to the paralysis, and he considers the application of paraffin and pressure suction the most suitable form of treatment. Fifty-four cases were treated by the author with underwater exercises in a pool the temperature of which was 92° F. This form of treatment was found to give the patients a sense of security and enjoyment; the effect of gravity was eliminated so that the weight of an extremity did not overstretch a weakened muscle. The motion through water produced an excellent form of massage, and the circulatory deficiency was supplied with evenly distributed moist heat. One half of these patients were admitted when muscle soreness had disappeared, and the other half about 6 months after the acute onset. Those patients admitted earlier showed almost twice as much improvement as those admitted later, and the results obtained were considered encouraging.

Ashley, R. F. (1939) *Arch Otolaryng*, Chicago, **29**, 104.

Casassa, A. (1938) *Bull. Acad Méd Paris*, **120**, 124.

Hanson, K. G. (1939) *J. Amer. med. Ass*, **113**, 32.

Schultz, F. W. (1938, a) *J. Pediat*, **13**, 38.

— (1938, b) *Amer. J. Surg*, **42**, 178

Tisdall, F. F., Brown, A., and Defries, R. D. (1938) *J. Pediat*, **13**, 60

POST-MORTEM EXAMINATION

See also Vol X, p 28, and Cumulative Supplement, Key Nos 1283–1290

Blood stains

The ordinary methods of detecting blood in medico-legal practice are useless if the sample has been subjected to high temperatures. A. M. Moody *et al.* examined microscopically blood which had been heated to 1,600° F. (871° C.) and found that dried blood melted at 500° to 515° F., and assumed a characteristic structure above 700° F. In this microscopical appearance, called 'ring-structures', the red blood corpuscles presented a number of constituents shaped not unlike the models used for teaching the molecular structure of substances. These ring-structures were visible even when very small quantities of blood were available and if the blood had been mixed with some other substance, such as grass. Other incinerated organic substances of large molecular structure, such as egg white, showed characteristic heat structures, but they could easily be distinguished from those of blood.

Moody, A. M., Proescher, F., and Carr, J. L. (1938) *Arch Path*, **26**, 501.

Subclinical Lesions

In a short but suggestive article on subclinical lesions of the body, H. E. Robertson criticized the wide-spread conclusion that absence of clinical manifestations necessarily means freedom from morbid changes. The first question put to a patient was naturally how long have you been ill; but from the point of view of morbid changes present neither the patient nor the practitioner could answer this question accurately. It was not possible clinically to detect evidence of the incubation stage of the exanthemata. A list was given of about 25 lesions, such as cysts in the choroid plexus, most pituitary adenomas, arachnoid opacities, chondromas, and anthracosis of the lungs, capsular lymphangiomas of the spleen, angiomas of the liver, lymphoid hyperplasia of the ileum, thrombosis of the prostatic plexus, and chronic infarction of the testis, which might never have caused any signs or symptoms. Another collection of nearly 20 were submerged below the levels of clinical recognition for the greater part of their existence and had in fact a relatively long incubation period. Nephritis and hepatic cirrhosis might long be latent before appearing suddenly and running a rapidly fatal course. Many internal cancers started under adverse conditions of growth, and these inhibitory factors might keep the tumour process fairly stationary for years. Further, necropsies often showed the presence of a dozen morbid changes, other than the cause of death, in various stages of development.

Robertson, H. E. (1938) *Proc. Mayo Clin*, **13**, 734.

PREGNANCY. NORMAL AND PATHOLOGICAL.

See also Vol. X, p. 48, Cumulative Supplement, Key Nos. 1291-1303, and p. this volume

Diagnosis

Aschheim-Zondek Test

Aschheim stated that the amount of urine required to give a positive Aschheim-Zondek reaction in the presence of a hydatidiform mole was only one-twelfth of that needed for the reaction in ordinary pregnancy. M. Boycott and J. M. Smiles reported a case in which the level of the gonadotrophic hormone in the urine was so high as to suggest the presence of a hydatidiform mole. The patient, however, gave birth to a ten-inch foetus of 18 weeks' development and in the placenta there was no macroscopical or microscopical evidence of mole formation. Boycott and Smiles then investigated the level of the gonadotrophic hormone in the urine of 5 antenatal patients. They found that the level is often higher than is usually supposed and highest at that stage of pregnancy when a hydatidiform mole is likely to be suspected.

In the opinion of the authors, the maximum is usually between the eighth and the tenth week. High values are found in all forms of vomiting of pregnancy. In 2 cases of hydatidiform mole the Friedman test was negative with very small quantities of urine. Boycott and Smiles therefore concluded that the diagnosis of hydatidiform mole cannot be made on the level of the gonadotrophic hormone in the urine alone.

*The *Xenopus* Pregnancy Test*

I. R. Elkan described the *Xenopus* pregnancy-test as an alternative to the Aschheim-Zondek or the Friedman techniques. The toad *Xenopus laevis* Daud is fairly common in all the tropical parts of Africa and is exported freely from Cape Town. The adult clawed toad varies in size from 2 to 4½ inches, the medium size being the most suitable for the test. Like other methods, the test depends on the response of the animal's gonads to the anterior-pituitary-like hormone in the urine of pregnant women. The specific gravity of the



FIG. 20.—Dissection of a female *Xenopus laevis* which was kept in captivity for over six months and then killed after having given a positive pregnancy test reaction. Note the well-developed ovaries and oviducts and the absence of any signs of degeneration of the reproductive system. (From *British Medical Journal*, 1938)

urine should be between 1020 and 1030, for reliable results could not be expected from urines with a specific gravity below 1015. For the test 2 c.cm. of untreated urine or 1 c.cm. of an extract made by Zondek's alcohol and acetone precipita-

tion method was injected into the lymph sac under the dorsal skin of a variable number of female toads. After the injection, the toads were put into test jars kept at a temperature of 26° C. where they sat on perforated platforms so that they had no chance of eating their own spawn. The time between injection and oviposition varied between 5 and 12 hours. In the jar the eggs either stuck to the underside of the platform or fell to the bottom of the jar. Their number varied enormously; 5 to 6 eggs or upwards might be counted a positive reaction. Tests in which only one or two eggs had been laid by one or two toads should be repeated and were usually found to be negative. In the absence of males, these eggs were necessarily unfertilized. The animals were left in their jars overnight and results were read the next morning. The animals after the result had been read were kept in the testing tank for a week if the test was negative, and for a month in the case of a positive test. The test should be reserved for patients who have passed the first 'missed' period by at least 2 to 3 weeks. The test, which gave the result in 24 hours, was as reliable as the Aschheim-Zondek and Friedman reactions; in 295 tests, with the use of 2,112 toads, a definite positive for pregnancy had always been proved to be correct.

Antuitrin-S Skin Test

A skin test for pregnancy based on the idea that an anterior-pituitary-like substance is present in the circulation of pregnant women and renders them insensitive to intradermal injections of the substance was sponsored by Gillfillen and Gregg and its claims investigated by S. R. Parsons. The technique consisted of the intradermal injection of 2 minims of antuitrin-S in the flexor surface of the forearm. The reaction occurred within a few minutes and, in the non-pregnant, an erythematous area, up to 40 mm. in diameter, developed round the site of injection. The author experimented with 140 cases, other substances used being antophysin and follutein. She concluded that the test was entirely unreliable, the margin of error in the early months of pregnancy, when diagnosis is so important, being up to 70 per cent.

Boycott, M., and Smiles, J. M. (1939) *Lancet*, **1**, 1428

Ilkan, I. R. (1938) *Brit. med. J.*, **2**, 1253

Parsons, S. R. (1939) *Ing. Gynec. Obstet.*, **68**, 187

Determination of Viability of Foetus

Foetal Electrocardiography

This new method of determining whether or not the foetus is alive during pregnancy was described by E. O. Strassmann and R. D. Mussey. Seventy foetal electrocardiograms were recorded from 52 mothers during the last 10 weeks of pregnancy, 87 per cent were positive and 13 per cent were negative. During the last 20 days of pregnancy 91 per cent were positive. Five leads were taken with the woman in the supine position: (i) right arm-left arm, (ii) right arm-left thigh, (iii) left arm-left thigh, (iv) right arm-right thigh, (v) left arm-right thigh. These five leads covered the main directions in which the axis of the foetal heart might lie. The largest number of positive results were obtained in the 3rd and 5th leads because they are most favourable in the left vertex position of the foetus. The examination was of use in comparing the foetal and maternal hearts, determining the viability of the foetus, and examining the rate, rhythm, and regularity of the foetal heart action.

Strassmann, E. O., and Mussey, R. D. (1938) *Amer. J. Obstet. Gynec.*, **36**, 986

Hyperemesis Gravidarum

Aetiology, Pathogenesis, and Treatment

J. W. Finch worked on the hypothesis that nausea and vomiting during pregnancy are due to an allergic reaction of the patient to the secretion of her own corpus luteum of pregnancy. Hirst was the first to associate the nausea and vomiting of pregnancy with the functional activity of the corpus luteum. He stated that every woman during her menstrual life is constantly absorbing corpus luteum substance, but that with the onset of pregnancy this absorption ceases. In accordance with this view he gave corpus luteum extract to a number of patients with surprisingly good results in alleviating or even terminating their symptoms. The corpus luteum continues to develop with pregnancy, the colloid increasing and the granulosa cells

becoming larger than before pregnancy. By the fourth month retrogressive changes take place in the corpus luteum with consequent relief of symptoms. Finch tested patients by the intradermal injection from 0.02 to 0.03 c.cm. of progestin in sterile cotton seed oil and recorded the reaction 15 and 30 minutes later. Reactions were calibrated according to the size of the wheal and the degree of surrounding erythema. A control injection was made with sterile cotton seed oil in the same arm. Patients with nausea may have inherited a sensitivity to progestin. If other investigations should confirm these observations, it might be assumed that a patient desiring pregnancy could be tested for sensitivity to progestin and if found sensitive could be desensitized before impregnation. The treatment would consist of graduated doses of progestin injected at short intervals until the patient is desensitized and the symptoms either do not develop or are relieved if they do. It was suggested that some solvent in place of oil could be used for the tests in order to avoid skin irritation.

In a paper on the relation of pregnancy to biliary disease and the control of the vomiting of pregnancy J. M. McGowan and J. O. Baker have followed up their previous publications on allied subjects, which showed that spasm of the second part of the duodenum closed the lower end of the common bile-duct. This result could be produced in normal subjects by the hypodermic injection of morphine sulphate $\frac{1}{4}$ grain, and relieved promptly and completely by the inhalation of amyl nitrite, and partially by administration by the sublingual route of $\frac{1}{100}$ grain tablets of glyceryl trinitrate (nitroglycerin). Possibly there was some endocrine excess which tended to cause the duodenal spasm to be exaggerated in pregnancy. In 12 patients with vomiting of pregnancy glyceryl trinitrate was consistently successful in giving relief usually within 3 days, but it was mentioned that it might not be effective in very severe cases. The tablets were taken after a meal, which should be full and mixed in composition, and as there was a slight fall of blood pressure the patients should lie down for 10 minutes after taking the tablets, of which as many as 12 have been taken in the 24 hours without toxic effects. It was suggested that duodenal spasm was a cause of hyperemesis gravidarum. Post-cholecystectomy colic had responded well to glyceryl trinitrate. Repeated duodenal spasm by causing biliary obstruction might help to explain the tendency of pregnancy to cause disease of the biliary tract.

Finch, J. W. (1938) *J. Amer. med. Ass.*, **111**, 1368.

McGowan, J. M., and Baker, J. O. (1938) *Canad. med. Ass. J.*, **39**, 133.

Toxaemias of Late Pregnancy

Preeclamptic Toxaemia and Eclampsia

Clinical picture—Abnormal increase in weight during pregnancy has been regarded as such a reliable sign of toxæmia of pregnancy that the latter could be diagnosed from it alone. From an investigation of 100 cases with definite toxæmia of late pregnancy, R. S. Sidall and H. C. Mack conclude that an excessive increase of weight is of doubtful value as a warning of the toxæmia of pregnancy and only of secondary importance in its diagnosis. Their cases had an average gain of 17 pounds during the last 4 lunar months of pregnancy compared with the normal 15.7 pounds. Of their 100 patients 61 showed gains of weight at least twice the average of controls at one or more observation periods during this time, but a similar gain in weight also occurred in 45 per cent of the normal pregnancies. Sudden increase of weight was somewhat more frequent among toxæmic than among normal pregnancies, but was far from constant. The presence or absence of excessive gains in weight did not bear any relation to the type or severity of the toxæmia.

Diagnosis—V. I. Krieger reviewed the renal function tests with special reference to their use in the toxæmias of pregnancy. She found that the Van Slyke urea clearance test, the urea concentration test, and the Rabinowitch factor tests were not reliable for the estimation of renal function in pregnancy. The last test was found to give incorrect results when small volumes of urine with high urea concentrations, or large volumes of urine with low urea concentrations, occurred. However, the Fowweather urea clearance test and the urea concentration-excretion test were found to give excellent results in the assessment of the renal function, agreement between the two occurring in 67 per cent of the tests performed.

The cold pressor test—The cold pressor test is carried out by first resting the patient in a chair or in a semireclining position in bed, if possible for one hour, in a room in which all extraneous noises and distractions are reduced to a minimum. A blood-pressure reading is then made. If the patient cannot rest for so long, readings

are made at intervals of 2 or 3 minutes until a basal reading is obtained. The extended hand of the arm wearing the blood-pressure cuff is immersed up to the wrist in iced water at 1° to 2° C. The blood pressure is taken immediately, then every 30 seconds for 2 minutes, when the hand is removed. The blood pressure is then taken at 3-minute intervals for 15 minutes to note the time it takes to return to the normal level. W. J. Dieckmann *et al.* investigated the test in 152 normal pregnant women. An increase in systolic pressure of 30 mm. or more was considered to be abnormal. Ninety patients were hyper-reactors, of whom 15 developed toxæmia and an additional 13 exhibited transient vascular renal signs. In 62 patients a normal response occurred and of these only 2 developed toxæmia.

Treatment.—H. Mittelstrass reported on his investigations on the treatment of eclampsia and its premonitory symptoms with short waves. Microscopical examination of the capillaries of the finger-nails in cases of eclampsia almost always showed a disturbance of circulation which after short-wave irradiation of the kidneys returned to normal. On the other hand, irradiation had no marked effect on eclampsia and the author therefore did not agree that arterial spasms were of importance in the aetiology of eclampsia. Irradiation of other regions, such as the carotid sinus, was also of no value and no changes were observed on retinoscopy after athermic irradiation of the head. Short waves, however, were of value in treating post-eclamptic symptoms, such as persistent oliguria.

Essential Hypertension

Clinical picture.—J. F. Schultz and C. S. O'Brien made careful studies of the retinal changes observed in the hypertensive toxæmias of pregnancy. These changes were closely associated with the blood-pressure level and in a group of 47 pregnant women retinitis was observed in 12 patients whose blood pressure on admission to hospital varied from 170 to 230 mm. Hg systolic and 110 to 160 diastolic. Nine days after delivery, the blood pressure, although still high, was considerably reduced and ranged from 120 to 215 systolic and 82 to 135 diastolic. It was considered that this group was more seriously affected than any other and that the prognosis was poor. In 3 cases retinal detachment was present on admission but 4 months after delivery the retina had re-attached in each case. Visual disturbances were found only in 15 patients. Other changes noted were angiosclerosis in 12 patients and angiospasm of the retinal arterioles in 13. Of the latter 4 had normal fundi on discharge and 5 others were found to be normal after a period of 4 months. It was concluded from this that, when angiospasm was observed, if suitable treatment was instituted the patient generally made a good recovery. The authors considered that, if indications of organic change appeared in the retina or vessels, emptying of the uterus was advisable.

- Dieckmann, W. J., Michel, H. L., and Woodruff, P. W. (1938) *Amer. J. Obstet. Gynaec.* **36**, 408.
 Krieger, V. I. (1938) *Med. J. Aust.*, **2**, 457.
 Mittelstrass, H. (1939) *Klin. Wschr.*, **18**, 775.
 Schultz, J. F., and O'Brien, C. S. (1938) *Amer. J. Ophthal.* **21**, 767.
 Siddall, R. S., and Mack, H. C. (1938) *Amer. J. Obstet. Gynaec.* **36**, 380.

Diseases of the Cardiovascular System

Heart Disease

G. W. Parade summarized the modern German views on valvular disease in pregnancy. Increased strain was imposed on the circulatory system during pregnancy and it could be generally assumed that the heart of pregnant women acted in much the same way as that of untrained individuals performing unusual physical strain. Women with valvular disease fell into 3 categories: (i) those with compensated valvular conditions, about 60 to 70 per cent of all cases; (ii) those in which compensation was not well established, 15 to 20 per cent; (iii) decompensated hearts, making 10 to 15 per cent of the total. The first group had practically no difficulties to fear, except when the woman was unconscious of the condition and consequently did not take any special care. Medical supervision without any special treatment was all that was required in this group. In labile compensation, oedema and dyspnoea usually appeared soon after the early months of pregnancy and therefore a protracted digitalization was necessary. In the third group, medical treatment must aim at the restitution of the heart to the compensated stage and if, after several attempts, this failed, pregnancy must be interrupted. In any case of valvular disease, however,

the family should be restricted to one or few children only, as statistics showed that parous women with valvular disease were more prone than nulliparous women with valvular disease to early heart failure.

T. R. Turino and A. T. Antony studied 150 pregnancies in 110 women (81 primiparae and the others multiparae—para 2 to para 13) with organic heart disease. Left occipito-anterior was the commonest foetal position and other lies were not encountered more often than in normal women. They found that labour was not, as is commonly supposed, shorter than normal. The length of the second stage was often considerable and it was sometimes necessary to shorten it surgically to avoid overtaxing the damaged heart. The incidence of operative interference in this series was increased. Turino and Antony also considered that the first stage of labour may be very arduous through pain and fatigue, and to prevent too much strain being thrown on the heart they recommended that some analgesic, preferably morphine, should be given at this stage. For delivery they found open ether was the anaesthetic of choice. The incidence of premature labour was high in this series. The weight of the babies born was slightly above average. The foetal mortality was 10.4 per cent and the maternal 7 per cent; 5 of the women who died had not had antenatal care.

Varicose Veins

Treatment. J. Siegler describes a method of treatment for varicose veins in pregnancy which he used successfully in more than 125 cases. The technique consists of sterilizing the skin with 70 per cent alcohol and injecting 10 c.cm. of a solution of equal parts of 30 per cent sodium chloride and 50 per cent glucose into the affected vein. After injection a dry gauze sponge is applied to the site and kept in position with adhesive strapping. The injections are continued at weekly intervals or even more often until all affected veins have been treated. There is no limit to the number of injections that may be given. Varicosities of the vulva may be similarly treated and are usually obliterated after one injection. A type of varicosity peculiar to pregnancy consists of a collection of veins, purplish-blue in colour, communicating with a single vein which is not particularly enlarged. No cases of post-partum phlebitis occurred in this treated group, and immediate relief from symptoms was obtained by injections.

Parade, G. W. (1939) *Munch. med. Wschr.*, **86**, 681.

Siegler, J. (1939) *Amer. J. Surg.*, **44**, 403.

Turino, T. R., and Antony, A. T. (1938) *Amer. J. Surg.*, **41**, 453.

Diseases of the Nervous System

Polyneuritis

Treatment. In a severe case of polyneuritis during pregnancy, A. Hildebrandt and H. Otto used altogether 1,782 mg. of vitamin B₁ with excellent results and without any ill effects. Vitamin B₁ (betabion) was given intravenously in a daily dose of 2 mg. for 11 days and 10 mg. B₁ daily for 35 days; 200 mg. of vitamin C daily were also given intravenously and later by mouth. Whereas there was a definite deficiency in the urinary excretion of vitamin B₁ and C before treatment, there was a normal excretion at the time of child-birth and later. The trial of vitamin B₁ in every case of polyneuritis during pregnancy, even if there is severe paralysis, was advised.

Hildebrandt, A., and Otto, H. (1938) *Munch. med. Wschr.*, **85**, 1619.

Vulvovaginitis in Pregnancy

Investigations were carried out by L. G. Waters and E. W. Cartwright to ascertain the incidence of monilial vulvovaginitis during pregnancy. In a series of 500 cases monilia was present in 54, or 10.8 per cent. Of these 54 only 5 complained of discomfort, which consisted of pruritus. Of the remaining 446 women, 14 (3.1 per cent) complained of pruritus. The only 3 cases of thrush which occurred in this series were in infants whose mothers showed no moniliasis. Three patients in the moniliasis group showed morbid symptoms and 35 in the non-moniliasis group. The pH was similar in both groups, the averages being 4.35 in the group without monilia and 4.33 in the group in which the fungus was present. The lochial flow seemed to inhibit the growth and the vagina was free of infection within 8 to 14 days post partum. The suggestion is made that abundance of glycogen in an acid medium is ideal for the growth of yeast cells. These requirements are fulfilled in the vaginal mucosa during pregnancy, when the cells are filled with glycogen, desquamation takes place

and the glycogen is converted into lactic acid, with a resulting vaginal secretion of low pH.

Waters, E. G., and Cartwright, E. W. (1939) *J. Amer. med. Ass.*, **113**, 30.

PREMATURITY

See also Vol. X, p. 126.

Feeding

Vitamin B₁

It has been shown experimentally that the vitamin B complex aids the retention of fluids. H. R. Litchfield *et al.* suggested that it might be useful in the treatment of marasmic and premature infants who require much fluid. Other investigators have found that there is too little vitamin B₁ in both breast and cows' milk for the infant's requirements and that it is diminished still further by boiling. Lack of vitamin B also leads to lack of growth in children. The authors gave yeast extract to 58 premature babies. A control group of 52 babies living under exactly the same conditions was observed. One teaspoonful (100 international B₁ and 40 Sherman-Bourquin B₂ units) was given twice daily in orange juice until a considerable gain in weight was recorded, when the dose was reduced to about 15 drops twice daily. The infants given yeast gained weight much more quickly than those without it; 55 per cent of them gained during the first week of life compared with 8 per cent in the control group, 95 per cent showed a gain at the end of two and a half weeks compared with 48 per cent in the control group. Infants with birth weights under 1,500 g. were 4 or 5 times their birth weight when infants in the control group had only doubled or trebled their weight. Twice as many infants whose birth weight was under 1,500 g. trebled their weight in 3 months as compared with infants who received no yeast extract.

Vitamin C

According to K. Jaroschka there is further scope for the employment of vitamin C (ascorbic acid) in infancy. Normally infants have a high vitamin C reserve which enables them to cope with their requirements, but in premature infants this reserve is much below the normal. The highest monthly incidence of prematurity (17 of 147) was observed during April, high figures also being recorded for March (13) and May (14). Some cases at least of prematurity are caused by a low vitamin C intake of the mothers. The author added vitamin C in large doses (0.5 g. ascorbic acid per day for 2 weeks) to the food, and in breast-fed children 100 mg. of vitamin C was given to the mother. In severe cases 0.025 g. of ascorbic acid was injected subcutaneously. The mortality of premature infants, previously 42 per cent before the introduction of ascorbic acid treatment, was reduced to 8 per cent.

Jaroschka, K. (1938) *Munch. med. Wschr.*, **85**, 1871.

Litchfield, H. R., Lichterman, J., Knolland, I., and Kurland, I. (1939) *Amer. J. Dis. Child.*, **57**, 546.

PROSTATE DISEASES

See also Vol. X, p. 146, and p. 158 of this volume.

Simple Enlargement

Actiology

G. Petit *et al.*, as the result of experiments during 3 years, reported that in young dogs daily injections of oestradiol benzoate for 12 to 15 days in doses of 1,000 to 2,000 I.U. produced a temporary excess of oestrin in the blood and very definite glandular proliferation in the prostatic urethra and the prostate. The maximal dosage employed was 2,000 I.U. and the average 1,000 I.U. From being in a resting almost embryonic state the prostate rapidly reached its adult condition and showed adenomatous and cystic changes which were illustrated by a number of photomicrographs. Without concluding that the changes produced in young dogs were identical with those in senile prostatic enlargement in man, the research showed the extraordinary changes produced by the oestrogenic hormone. In the

discussion following the demonstration M. Chevassu, while agreeing that oestrin transformed the infantile into the adult prostate, insisted that the changes thus produced were not the same as those in the senile enlargement in man.

M. Muschat *et al.* investigated the creatinine retention in normal males at various periods of maturity; in eunuchs; in males with infantile genitalia; and in aged men with complete loss of sexual functions. Normal adult males show creatinine retention below 13 per cent while eunuchs show between 35 and 50 per cent. In the normal male after the age of 50, there is a notable decline in gonadal activity. Using the creatinine retention test, the gonadal activity in prostatic hypertrophy does not appear to be diminished but remains similar to that of the normal male adult. It is assumed that, if gonadal activity persists in spite of expected physiological decline, an enlargement of the prostate will ensue, and the administration of more male sex hormone may prove injurious in promoting increased growth of the already enlarged prostate.

Clinical Picture

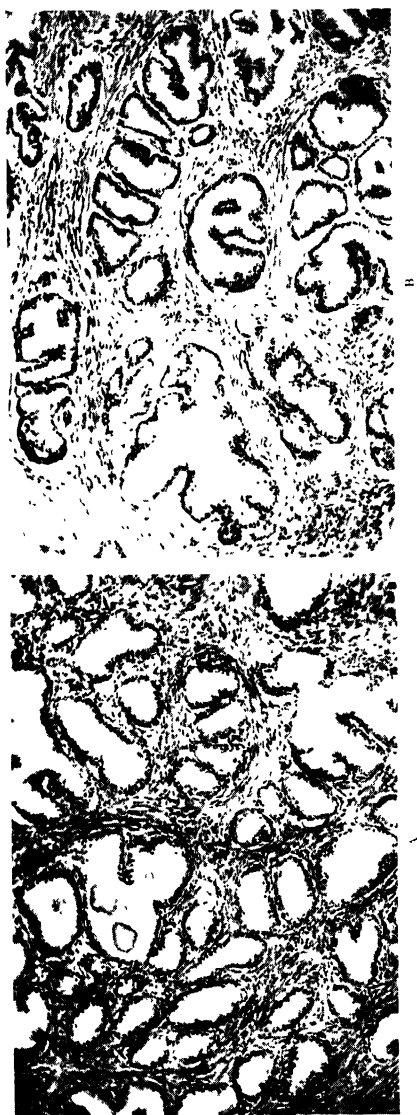
Measurement of residual urine.—In view of the fact that the decision for the performance or non-performance of prostatic resection is chiefly based on the amount of residual urine after voluntary micturition, T. J. Kirwin and G. A. Hawes urge a standardization of the methods for estimating and determining this quantity. With this end in view 3 series of experiments were undertaken: the first of 6 cases without vesical neck obstruction; the second of 13 cases, with vesical neck obstruction; and the third of 3 cases, in which determinations were made at 15-minute intervals. The latter class was recruited from 2 of series I and one of series II re-examined. The authors conclude that, in all cases, several determinations of the amount of residual urine should be made, at varying intervals, and that the psychic factor of anxiety, with its corresponding physical reaction of partial detrusor muscle paralysis, should be considered. Passage of a metal catheter or a cystoscope sheath is advisable, but it is pointed out that demonstration of residual urine is not by itself sufficient indication for the performance of vesical neck surgery.

Treatment

Testosterone propionate.—E. P. Sharpey-Schafer and R. Shackman described the case of a labourer, 53 years of age, with nocturnal frequency and slight haematuria caused by an enlarged prostate. After suprapubic drainage, 100 mg. of testosterone propionate in oil were injected daily for 34 days—a total of 3,400 mg. At the end of that period the prostate, which had shrunk to one-third of its previous size, was enucleated with some difficulty. The patient, seen 3 months later, was free from urinary symptoms. Histological examination of portions of the gland at both operations revealed no striking changes as the result of the testosterone propionate therapy (see Plate VI). The decrease in size of the gland was not necessarily accepted by the authors as being due to the injections, as it might well have been spontaneous or have followed the suprapubic drainage.

Intravenous sodium bicarbonate solution.—H. Retlev-Abrahamsen and V. Aalkjaer reviewed the condition of prostatic hypertrophy with reference to impaired renal function and disturbed fluid balance, as represented by increased blood-urea and diuresis. Patients with renal inadequacy and generally considered as true uraemia have, by systematic investigations, been proved to be suffering from acidosis, treatment of which has resulted in such improvement that operation is justifiable. Some patients with prostatic hypertrophy showed reduced plasma bicarbonate values, i.e. an acidosis, and the authors therefore gave intravenous injections of isotonic sodium bicarbonate solution, the doses being decided on the results of blood analysis and the patient's weight; they recommended that this alkali treatment should be restricted to hospitalized patients and only administered on the basis of frequent analyses of the plasma. As a result of their findings they consider examination for, and treatment of, the nephrogenic acidosis as indispensable in prostatic surgery.

Surgical.—In a series of 741 prostatectomies performed by E. Davis the mortality rate was only 2.7 per cent. In the last 144 of these, there was only one death. Such favourable results were obtained by a technique involving the combined use of perineal prostatectomy and irrigation of the urethra and bladder with a 2 per cent mercurochrome, alcohol, and acetone solution immediately prior to operation, and flushing of the wound with the same solution just before closure. This method was not expected to produce sterilization of the wound but results showed that it had an antiseptic effect. Instead of the usual post-operative temperatures averaging



Photomicrographs of sections of prostate removed by biopsy. A, before, and B, after treatment with testosterone (haematoxylin and eosin—60) (from *The Lancet*, 1939)

PLATE VI

101.5° F. the average maximal level was 100.2° to 100.6° F. For the prevention of haemorrhage a combined haemostatic and drainage bag which made it possible to visualize the under-surface of the neck of the bladder, was successfully used. Delayed haemorrhage has not been observed in the author's cases for a number of years. The suggestion is made that the above technique of wound antisepsis, with endoscopic fulguration, has helped to eliminate this complication. The sacral block method of anaesthesia is advocated and it has been noted that cases of post-operative shock rarely supervened when this method of anaesthesia was employed in perineal prostatectomy.

Davis, E. (1939) *J. Amer. med. Ass.*, **112**, 2485.

Kirwin, T. J., and Hawes, G. A. (1939) *J. Urol.*, **41**, 413.

Muschat, M., Labess, M., and Meranze, D. (1938) *J. Urol.*, **40**, 805.

Petit, G., Gley, P., and Bérault, E. (1939) *Bull. Acad. Méd. Paris.*, **121**, 430.

Retlev-Abrahamsen, H., and Aalkjaer, V. (1938) *Brit. J. Urol.*, **10**, 231.

Sharpey-Schafer, E. P., and Shackman, R. (1939) *Lancet*, **1**, 1254.

Malignant Disease

Carcinoma

From a large number of prostate glands, yielding 195 cases of primary carcinoma, J. F. Kahler drew the following conclusions: among men aged 50 or over primary carcinoma of the prostate occurs in 17.3 per cent, other authors have estimated this incidence between 14 and 21 per cent, and in men above 60 as 25 per cent. Only 53 per cent of the 195 carcinomas were recognized macroscopically at necropsy. Of the carcinomas 6 (or 3 per cent) were squamous-celled, all the others being adenocarcinomas. Of the carcinomas recognized clinically or grossly at necropsy 51 per cent showed metastases in the lymphatic glands, lungs, and pelvic peritoneum, in that order of frequency. The majority of the cases escape recognition clinically, and grossly at necropsy. There is not any relation between prostatic carcinoma and associated atrophy, nodular hypertrophy, inflammation, and calculi.

Rhabdomyosarcoma

P. Katzen *et al.* reported a case of rhabdomyosarcoma of the prostate in a boy aged 2½ years. This was the 12th recorded example of this rare form of tumour, which may have arisen from the striated muscle fibres normally present in small numbers in the gland. Sarcoma is a very rare tumour, occurs most often in the first decade of life, and is relatively commonest during early infancy. The total number of cases of sarcoma of the prostate now recorded is 152. It is usually a round-celled sarcoma, growing rapidly, often reaching a large size, and spreading by extension into neighbouring structures. Metastases occur, most often in the lungs and bones. Symptoms of urinary obstruction dominate the clinical picture. Pressure on the great veins of the pelvis and on the rectum produces oedema of the legs and ribbon stools. The disease has a rapid course and may end in uraemia. Diagnosis by rectal examination and by X-ray examination of the hydro-ureter and hydronephrosis produced by the urinary obstruction is easy in children. All methods of treatment have failed and surgery should be limited to the relief of symptoms, e.g. draining the bladder. X-ray and radium therapy prolong life.

Kahler, J. E. (1938) *Proc. Mayo Clin.*, **13**, 589.

Katzen, P., Cohen, H., and Steiner, M. A. (1938) *Amer. J. Dis. Child.*, **56**, 321.

Effects of Prostatic Massage

After prostatic massage some patients show mild or considerable vasomotor collapse. H. J. Hammer and T. S. Schulte analysed these reactions in 378 unselected cases, in 4 only of which syncope occurred. In 89, or 23 per cent, there was a decrease in both systolic and diastolic blood pressures, in 284, or 75 per cent, an increase in systolic or diastolic pressures. All the patients showed a rise in the pulse rate, on an average 16 per minute. In 36 patients over 60 years of age the average rise of blood pressure was much more prominent than in the other patients, and the subjects of essential hypertension showed a similar sensitivity to prostatic massage.

Hammer, H. J., and Schulte, T. S. (1939) *Proc. Mayo Clin.*, **14**, 13.

PRURITUS AND PRURIGO (HEBRA)

See also Vol X, p. 165

Pruritus Ani*Treatment*

Mercuric sulphide tattooing.—Many chronic cases of pruritus ani are primary in origin and the skin around often becomes secondarily infected with bacteria and mycelia. F. Hollander treated 24 cases of chronic primary pruritus ani as well as some cases of pruritus vulvae and pruritus scroti by tattooing with cinnabar (mercuric sulphide). All the patients recovered and have remained well over a period of months, and in 2 cases over one year. The skin was first shaved, surgically cleansed, and anaesthetized with 20 to 30 c.cm. of a 1 per cent solution of procaine hydrochloride. Phenolated soft paraffin was then rubbed into the skin and about the anal canal to ensure asepsis. An electric tattoo machine was used and the mercuric sulphide, mixed with sterile water to form a syrupy suspension, tattooed into the corium. One treatment, involving the skin one inch in front of the anus and the intertriginous line which is generally found in the midline of the intergluteal space posteriorly, was usually sufficient. No pain was felt but the patient should be given sedatives and liquid paraffin for a few days after treatment.

Hollander, I. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 337

PSITTACOSIS

See also Vol. X, p. 175

Aetiology

The isolation by mouse inoculation of the virus of psittacosis from a Bengalese finch imported into New South Wales is reported by A. R. Tremain. The strain appeared to be of low virulence, but this was enhanced by animal passage, killing mice on the third and fourth day, some 2 months after the initial inoculation. This is believed to be the first isolation of this disease in New South Wales and the first of its kind from a bird imported into Australia. The symptoms of the acute infection included lassitude, ruffling of feathers, fits of shivering, wasting of the pectoral muscles, nasal obstruction with consequent impairment of breathing, and sometimes diarrhoea. At necropsy the liver was large, heavy, and pale, sometimes being studded with infarcts or necroses. The enlarged spleen was congested and there might be patches of pulmonary pneumonia. According to Levinthal the budgerigar becomes a healthy carrier.

Tremain, A. R. (1938) *Med. J. Aust.*, **2**, 417

PSORIASIS

See also Vol X, p. 187, and Cumulative Supplement, Key No. 1312

Treatment*Low-Fat Diet*

It is generally accepted that psoriatic scale has a high cholesterol content. J. F. Madden limited the fat in his hospital dietary scale to 20 g. daily for adults and 10 g. daily for children, the caloric requirements being met by additional carbohydrate and protein. No ill effects were noted from the reduction in fat and in 70 per cent the low-fat diet was of definite value. In 3 cases the psoriasis entirely disappeared in 6, 7, and 24 weeks respectively, after this innovation. Other cases showed varying degrees of more or less temporary improvement. The stay of the patient in hospital seems to have been the most important factor in determining the effect of the diet on the disease. The favourable effect of the diet may be explained on the basis of a general realignment of metabolism and tissue function rather than on the basis of disturbed fat metabolism.

Madden, J. F. (1939) *Arch. Derm. Syph., N.Y.*, **39**, 268.

PSYCHIATRY OF CHILDREN

See also Vol. X, p. 203.

Behaviour Disorders

K. K. Cutts and H. H. Jasper studied 12 behaviour-problem children between the ages of 7 and 10 whom they called epileptoid, because their personalities and electro-encephalograms were similar to those of epileptic patients. One patient had a family history of epilepsy, only one had had fits. An electro-encephalogram was taken and repeated after the patient had been receiving 20 mg. of benzedrine sulphate daily for 6 days. A further examination was made after the addition of 1½ gr. of phenobarbitone each day for 3 days, and a fourth examination was made after the administration of phenobarbitone alone for 2 days. Half of the patients showed marked improvement in behaviour with benzedrine therapy. Phenobarbitone made most of the children worse and is therefore definitely contra-indicated in this disorder. The clinical changes produced by these drugs did not produce any constant corresponding changes in the electro-encephalogram, though those improved by benzedrine showed a prominent 6-cycle rhythm in the electro-encephalogram.

Cutts, K. K., and Jasper, H. H. (1939) *Arch. Neurol. Psychiat.*, Chicago, **41**, 1138

PSYCHONEUROSES AND PSYCHOTHERAPY

See also Vol. X, p. 232, and p. 116 of this volume

Psychoneuroses*Anxiety States*

Prognosis. An assessment of 259 cases which had been diagnosed as anxiety states between 10 and 12 years ago was attempted by A. Harris. A search was made for features of prognostic significance and for evidence of increased susceptibility to organic disease. A satisfactory follow-up was obtained in 48 per cent of cases. Of these, 31 per cent were well, 49 per cent were suffering from anxiety states, 7 per cent had developed psychoses, and 13 per cent were dead. The main prognostic points elicited were as follows. Anxiety and its clinical manifestations may persist unchanged for 10 years, and over, the percentage of cases in which it is converted to hypochondriasis being small. The prognosis is good if the condition is of less than 2 years' duration and, conversely, it is poor but not hopeless for ultimate and permanent recovery if the condition has been present for longer. The patient's chances of returning to work are always quite good, as only 20 per cent of those unable to work persisted in that state. When the patient's habits or mode of life remain unchanged by anxiety, the prognosis is good. The outlook in cases with markedly psychopathic personalities is poor. There was no evidence of increased susceptibility to organic disease in these patients.

Stage Fright

F. Volgyesi classifies stage-fright as a neurosis belonging to the group of diseases caused by a profession, and considers it the most classical sovereign human neurosis. From his experience the author feels that this type of neurosis reacts most successfully to treatment by psychotherapy with suggestive effects or hypnosis. A long protracted intense excitement of the motor nerves may gradually move the whole organism. A general pathological state of the psychological zones occurs, which is described as a panic-stricken feeling. 'The up-to-date verbal suggestive hypnotherapy, relieved of all superfluous trimmings and secrets, is the best of all modes of treatment.'

Adolescent Neuroses

According to E. Miller experience goes to show that there are two main types of disordered adolescent, the constitutionally sexually insufficient and the acquired psychically disturbed. Such incoordinations as occur at this time are primarily a product of ununified growth processes with excessive innervation in some types and reduced innervation in others. Those subjects who present the most difficult problem are the obvious misfits, either in their family atmosphere or in their cultural surroundings, or those who suffer these disadvantages in silence.

Relation of Neurosis to Gastro-Intestinal Disturbance

E. D. Bond discusses the relation of neurosis and gastro-intestinal disturbances. Emotional factors are largely responsible in many cases for colitis, both simple and ulcerative, for duodenal ulcers and even for vomiting and diarrhoea. Such cases often give a history of difficulties with early feeding and psychological conflict. Inversely, psychotic patients very frequently show gastro-intestinal disturbances, and instances are quoted of 4 cases of schizophrenia and one of involuntional melancholia. A psychiatric approach to the patient with vague gastro-intestinal symptoms should be made, not only in known psychotic and neurotic patients, but in all patients in whom unhappiness, tenseness, and frustration may be obvious or suspected

Bond, I. D. (1938) *Amer. J. digest. Dis.*, **5**, 482.

Harris, A. (1938) *Brit. med. J.*, **2**, 649

Miller, E. (1938) *J. ment. Sci.*, **84**, 1072.

Volgyesi, F. (1938) *J. ment. Sci.*, **84**, 1078.

Psychotherapy

D. Annau discusses 2 cases of severe organic disease which were markedly benefited by psychotherapy. The first was that of a young female with severe disseminated encephalomyelitis, who displayed the classical picture of a spastic paralysis with contractures and disturbances of micturition. Spontaneous movements of the legs were elicited, at first under hypnosis, and later without hypnosis. The organic condition remained unaltered. The second case was that of a hemiplegia with motor aphasia. This patient, emulating the success previously attained by another man, similarly afflicted, made strenuous and successful efforts. Sufficient evidence is forthcoming to show that the effects of organic injury are by no means absolute, and endeavours should be made by systematic psychotherapy, with help from the patient, to overcome any handicaps that may be present.

B. Stokvis maintains that every organ of the body in addition to its physiological function possesses a psychological one. For those suffering from circulatory disorders, psychotherapeutic measures which aim at soothing, quiet, and relaxation are recommended. A method of active relaxation is mentioned, for which the patient's co-operation is necessary. Certain exercises are performed at fixed hours. The tensograph was used for recording uninterrupted readings of the systolic and diastolic blood pressure, and the treatment controlled according to these findings.

Annau, D. (1938) *J. ment. Sci.*, **84**, 1089.

Stokvis, B. (1938) *J. ment. Sci.*, **84**, 1081.

PSYCHOSES: AFFECTIVE PSYCHOSES

See also Vol. X, p. 267, and p. 118 of this volume.

Aetiology*Relation to Diabetes Mellitus*

Fribourg-Blanc described a case of melancholic depression in a patient with diabetes mellitus and its successful treatment with insulin. The action of the liver on the development of mental changes has long been known and the author points out the possibility of a frequent connexion between hepatic insufficiency and the manic-depressive cycle. In this case the psychic condition and its treatment by insulin led to the discovery of the patient's latent diabetes.

Fribourg-Blanc (1939) *Bruux. méd.*, **19**, 1051.

Treatment*Insulin-Shock Therapy*

D. V. Conwell and C. J. Kurth treated not only schizophrenics but also manic-depressives, melancholics, and psychasthenics with insulin. This was of great value in the treatment of schizophrenia and in the manic phase of the manic-depressive psychosis. It was helpful in psychasthenia but of questionable value in the depressed phase of manic-depressive psychosis and in melancholia. Some of the danger of insulin shock treatment could be removed by a low-carbohydrate diet, thus removing the necessity for large doses of insulin. This often decreased the functions of the

adrenal or thyroid with a tendency to modified gonadal function. There were not any immediate or late changes in the pituitary or the parathyroid.

Bile Acids and Vitamin B₁

H. Sopp drew attention to the importance played by the liver in the depressive syndrome, the manifestation of the cyclothymic mental aberration. The attempts at treatment of these conditions with bile acids was well known and the author carried this method a step further. Recollecting the part played by vitamin B₁ in the humoral control of the central nervous system, he combined the two principles and treated established cases of depression with both bile acids and vitamin B₁. The author administered for 4 days 10 c.cm. of decholin (dehydrocholic acid) daily with 1 ampoule of betabin (a vitamin B₁ preparation) intravenously or subcutaneously. Of the 32 cases treated, 18 showed a marked improvement. No improvement was effected in any case in which paranoid elements co-existed.

Conwell, D. V., and Kurth, C. J. (1938) *Endocrinology*, **23**, 767

Sopp, H. (1939) *Med. Klin.*, **35**, 710.

PSYCHOSES· SCHIZOPHRENIA

See also Vol. X, p. 302, and p. 116 of this volume

Aetiology

J. H. Quastel and W. T. Wales investigated faulty detoxication in schizophrenia by the hippuric-acid excretion test (Quick) after administration of benzoate, a method not previously employed systematically in the investigation of mental disease. The 67 cases of mental disorder he selected for this investigation had not been treated by arsenic or any drug exerting a toxic action on the liver, and in none was there evidence of hepatic or renal disorder. Forty-five patients thus tested were schizophrenics, and of these 18 were catatonics. The average amount of hippuric acid eliminated in the non-catatonic schizophrenic group, expressed in terms of benzoic acid, in 4 hours after the administration of 6.0 g. of sodium benzoate, was 3.4 g. with an average mean deviation of .04 g.; the excretion of hippuric acid was normal in 23 out of the 27 cases. The average value of hippuric acid eliminated under the same conditions by catatonic patients was 2.2 g. with an average mean deviation of .05 g., all the catatonic patients showing a diminished excretion of hippuric acid. It was inferred that a metabolic disturbance in the liver, affecting benzoic acid detoxication, might be partly responsible for the psychosis by damaging the nervous tissues of catatonic patients. Among the 22 non-schizophrenic patients, 12 being manic-depressives, several gave low rates of hippuric excretion.

Quastel, J. H., and Wales, W. T. (1938) *Lancet*, **2**, 301

Quick, A. J. (1933) *Amer. J. med. Sci.*, **185**, 630.

Prognosis

J. Gelpert undertook a survey of the number of spontaneous remissions in cases of schizophrenia. None of these had received cardiazol or insulin shock therapy at the Cincinnati General or State Hospital. Out of a total of 235 patients, 94 were discharged as improved. The only treatment which these patients had received was superficial psychotherapy. Thirty-five of these 94 patients were discharged straight from the general hospital. Twenty-one of these were traced and interviewed. Three returned to hospital, but the remaining 18 maintained their improvement and led a normal life, several of them working full or part time. The average duration of this improvement up to the time of interview was 25.9 months, the ability of adjusting themselves to a normal, communal existence being considered the criterion.

Gelpert, J. (1939) *J. Amer. med. Ass.*, **112**, 2393

Treatment

Cardiazol Convulsion Therapy

I. Atkin treated 12 female patients suffering from chronic schizophrenia with cardiazol (pentamethylenetetrazol). Morphine sulphate $\frac{1}{2}$ gr., hyoscine hydrobromide $\frac{1}{100}$ gr., and atropine sulphate $\frac{1}{150}$ gr. was given half an hour before

treatment in very restless patients. An attempt was made to induce a convulsion every fourth day and about 20 convulsions in all. There was a fortnight's interval in the middle of the course. Intravenous injections of triazol (*cyclo-hexylethyl-triazol*) were given, the convulsant doses ranging from 0.7 c.cm. to 2.3 c.cm. with initial effective doses of 1 c.cm. increased by 0.2 c.cm. at a time if no convulsion resulted. Intramuscular injections were used when no veins were available or when the patient was very restless, the convulsant doses here ranging from 0.9 c.cm. to 2.8 c.cm. and the initial doses from 0.9 c.cm. to 1.8 c.cm. Generalized muscular spasms appeared 5 to 30 seconds after the injection. After one minute in 79 per cent of treatments there was an epileptic fit. There were no complications other than one death from acute pulmonary tuberculosis resulting from reactivation of an old lesion following a fit. Three out of the 12 patients were benefited by the therapy, which indicates that this is of value in chronic schizophrenia when there is little hope of improvement by ordinary methods of treatment.

Mechanism of convulsion -- In an attempt to elucidate the mechanism of the convulsion following the administration of cardiazol, J. A. F. Denysen and D. J. Watterson experimented with appropriate doses of various vaso-depressant drugs -- amyl nitrite, sodium nitrite, and histamine, given immediately prior to the known convulsion-producing dose of cardiazol. The subjects were 32 schizophrenics in good physical health. These measures mainly prevented convulsions, demonstrating the fact that vasodilatation, under appropriate conditions, prevents their occurrence. The action of cardiazol on the cardiovascular and central nervous systems is reviewed, and it is concluded that cardiazol-produced convulsions are due to sudden vaso-constriction.

F. Reitmann analysed the results of American and European authors in the treatment of schizophrenia with cardiazol. The analysis was difficult owing to the different classifications adopted by individual authors and their varying assessments of what constituted a remission of the disease. Of full remissions the number was 52 per cent with a standard deviation from the mean of 3.8 per cent. This figure agrees with that of other observers. This remission-rate includes only acute and subacute cases as nothing but possible arrest of the disease can be expected in chronic cases and when the latter are of more than 6 to 7 years' duration the prognosis is hopeless.

Spontaneous fractures -- T. and V. Struppler collected the observations of various authors on the occurrence of fractures sustained in the course of treatment of schizophrenia with cardiazol. Meduna observed 1.4 per cent of fractures in the course of treatment of his patients, a phenomenon which puzzled neurologists for a considerable time. The authors observed that the usual course of a spasm elicited by cardiazol was as follows: immediately after the injection the patient becomes pale, and 9 to 85 seconds later the attack begins with clonic twitches, which develop into a tonic spasm. The body stiffens and uncoordinated movements are performed by the extremities. The mouth is held open for about 10 seconds, the pupils are wide and do not react to light, there is spontaneous micturition. Five c.cm. of 10 per cent cardiazol intravenously, the normal dose, produces such an attack which lasts about 35 to 80 seconds. The extreme hyperextension in the extensor muscles of the body is responsible for the fractures. This hypertonus of the extensors is so marked that fractures of the neck of the femur and of lumbar vertebrae were observed in a few cases in which direct injury or accident during the course of the spasm was eliminated.

Compression fractures of spine -- P. Polatin *et al.* found that whereas, following the cardiazol treatment in cases of schizophrenia, dislocations and fractures of the extremities have been freely reported, little attention has hitherto been paid to compression fractures of the thoracic vertebrae which constituted a frequent sequel. In this series 51 patients were studied, 20 being males and 31 females. The average age for the group was 29 years. Fractures, mostly in the mid-thoracic region, were found in 22 patients, of whom 6 (27 per cent) were males and 16 (73 per cent) were females. The number of segments affected varied between 3 and 4. Convulsions generally occurred following an injection of 4 to 6 c.cm. of cardiazol and treatment was given 2 or 3 times weekly. The maximal dose of cardiazol used was 11.5 c.cm. There was no relation between the number of seizures and the number of vertebrae affected. Many patients who complained of pain in the back manifested no bony injury, whereas males with fractures sometimes did not complain of pain. Radiographs of the fracture mainly showed a compression of the anterior part of the upper surface of the vertebral body. In about 50 per cent of the cases, a slight disk-like fragment of the upper part of the body was displaced forward. Accompanying

kyphosis and scoliosis were sometimes seen. To avoid such complications in the future, the authors think that cardiazol should be injected with the patient lying on his side and acutely flexed, thereby reducing any sudden flexion of the spine, a cause of vertebral injuries.

In the 8 cases of compression fracture of the spine complicating cardiazol therapy quoted by B. T. Bennett and C. P. Fitzpatrick the injury was confined to the dorsal vertebrae, and often to the fifth, sixth, and seventh. It was considered to be occasioned by the violent flexions of the body with both tonic and clonic convulsions. The pain associated with the fractures usually appeared early in the course of treatment and sometimes even after the first or second convulsion. In some cases localized tenderness to light percussion was present over the portion of the spine involved. Diagnosis was made by X-rays. Although the cases under review showed only slight disability from the spinal condition, it would seem impossible to foresee the end effects, which might result in definite kyphosis, due to further collapse of the vertebral bodies involved, or to further narrowing of the intervertebral spaces with disturbances of the intervertebral discs. Cessation of this form of treatment was advised until suitable preventive measures could be instituted. A modified curved Bradford frame, to which the patient could be strapped, was suggested as a form of support.

J. Valso drew attention to the occurrence of vertebral fractures in the course of treatment of psychotic conditions with cardiazol, which produces spasms of the muscular system. The scarcity of reports of this complication is due, in the author's view, to the relative absence of reliable clinical signs, and it is assumed that only by constant X-ray examinations will all vertebral fractures be diagnosed. The fractures occurred especially in the region of the thoracic vertebrae. A routine X-ray control of the skeletal system is therefore a necessity during treatment of psychoses with cardiazol.

Prevention of spontaneous fractures—Seven cases of spontaneous fractures occurred in patients receiving convulsive shock therapy, and W. R. Hamis and A. F. Bennett emphasize the necessity of their prevention in the course of a treatment which has been used so successfully in schizophrenia and allied conditions. Prophylaxis has been found useful, and consisted of giving an intraspinal injection of 10 mg. of pontocaine hydrochloride or 100 mg. of procaine hydrochloride, dissolved in 4 c. cm. of spinal fluid, obtained by puncture between the first and second lumbar vertebrae by means of a 22-gauge needle. This injection was given from half an hour to an hour before the cardiazol, and its effect lasted until about an hour after the convulsion. Having induced this anaesthesia, it remained only to attend to the upper extremities and, at the onset of each tonic spasm, the arms were held adducted against the chest wall. In view of the frequency of fractures sustained as a result of this treatment, the theory of bone atrophy as a concomitant of the existing disease is suggested.

Cardiac complications—Four cases of schizophrenia are reviewed by A. Dick and W. McAdam, 2 being hebephrenics and 2 of the catatonic type, all of whom received cardiazol treatment. All showed a normal cardiovascular system at the commencement of treatment, but as a result of the injections, 3 developed auricular fibrillation, and one temporary heart block. The first three cases had been given respectively 19, 25, and 18 injections and the possibility of cumulative action could not be excluded. Bi-weekly injections of a 10 per cent solution of cardiazol were employed, commencing with 3.5 or 4 c. cm. Treatment was stopped after the appearance of the cardiac irregularity, which seemed to be only temporary and cleared up following rest, without medication. The fourth case had only received 2 injections, given within a few minutes of each other, after each of which cardiac irregularities were noted. The first, second, and fourth case of this series showed mental improvement.

Factors which render treatment dangerous—M. Hayman and M. W. Brody reported the case of a man aged 24, with negative physical and laboratory findings, who died during the sixth treatment in a course of treatment by cardiazol. The necropsy showed marked congestion of all the organs and an old endocarditis. Reference was made to 3 previously reported deaths associated with cardiazol treatment in which pre-existing lesions were present: (i) aortic disease, (ii) bilateral hypernephroma and goitre, and (iii) pulmonary embolism and pelvic thrombophlebitis. In the presence of a minimal cardiac lesion the drug was not so innocuous as generally supposed; as a preliminary to the treatment, basal metabolic tests, X-ray examination of the chest, and electrocardiographic examination should be made in addition to thorough physical examination and routine laboratory tests.

Blood pressure—E. Guttman and F. Reitmann of the Research Unit of the Maudsley Hospital took blood-pressure readings from patients before the injection

of cardiazol, in the latent period before the fit, immediately after the fit, and at short intervals thereafter. The average blood-pressure curve, constructed from 15 such observations, showed an initial rise followed by a fall of blood pressure coinciding with the fit, and finally a steep rise which did not entirely subside to the initial line. Sub-convulsant doses of cardiazol (3 c.cm. of a 10 per cent solution) produced a rise of blood pressure reaching its maximum 2 minutes after injection; the nearer the dose to the convulsant threshold the higher was the rise of blood pressure. If the blood pressure was kept low by amyl nitrite, there was not a fit; but a sudden rise of blood pressure induced by an intravenous injection of 10 mg. benzedrine did not produce a fit with subliminal doses of cardiazol. This result militated against the possibility that the blood pressure was the causal factor in the production of the convulsion, and was in favour of a direct toxic action of cardiazol on the nerve cells.

Triazol Convulsion Therapy

F. J. Napier recorded the treatment by azoman (triazol 156) of 37 patients with psychosis, including (but not exclusively) schizophrenia, in which convulsion therapy was of value. Although cardiazol was immensely superior to the original camphor, it was not free from some serious disadvantages, and azoman, introduced by Walk and Mayer-Gross, is here recommended as an improvement on cardiazol in all psychoses in which convulsions are induced. The drug is supplied in ampoules of about 2.2 c.cm. of a 5 per cent solution, and may be given orally or by any of the parenteral routes. The dose varied according to route, being less intravenously and more by the mouth, the initial dose recommended being 1 c.cm. intravenously or double that intramuscularly. The interval between the administration and the onset was seldom less than half a minute intravenously, though when a minimal dosage was employed, it might extend to 2 or 3 minutes; when the drug was given intramuscularly, 10 to 20 minutes might intervene. An advantage of the use of azoman, in preference to cardiazol, was the close relationship between variation in dosage and variation in results, so that a reduction of 0.2 c.cm. might fail to induce a convulsion, whereas a similar increase might be followed by an unnecessarily vigorous convulsion. The fractures which occasionally occur (there were 2 in this series) were most probably avoidable if the convulsive threshold was not much exceeded. Dislocation of the jaw could be prevented if at the onset of the tonic phase hyperextension of the jaw was obviated. In one of the 37 cases the shoulder was dislocated. No complications other than those known to attend cardiazol convulsions have occurred in these cases treated by azoman.

Blood pressure.—In a research on the psychic and somatic reactions to sub-convulsive and convulsive doses of triazol on two groups of 12 patients each: (i) schizophrenic, (ii) a heterogeneous group of other disorders, J. B. Dynes and H. Tod found that the pulse-rate, blood pressure, and pulse pressure showed definite evidence of stimulation in both groups after sub-convulsive doses of triazol without any significant difference in the 2 groups. After a convulsion the schizophrenic group showed almost twice as great a response as did the heterogeneous group. This might mean that the schizophrenics failed to maintain homeostatic conditions under stress; they required appreciably less triazol to produce a convulsion than did the heterogeneous group.

Picrotoxin Convulsive Therapy

A. A. Low *et al.* used picrotoxin as a therapeutic convulsant in the treatment of mental illness in the search for a substitute for cardiazol which would avoid its frightening effect. In animals, the minimal convulsant dose is one-third to one-half of the minimum lethal dose, and sodium amylal injected intravenously is an efficient antidote. Thirty-eight patients completed a course of the treatment. Of these 19 were schizophrenics, 8 manic-depressives, 7 psychopaths, and 4 behaviour abnormalities. The schizophrenics were an unfavourable group in so much as the average duration of the disease prior to admission was 30 months. The recovery rate for the schizophrenics was 26.3 per cent, for the manic-depressives 62.5 per cent, for the psychopaths 71.4 per cent (14.3 per cent of these being social recoveries only), and for the behaviour abnormalities 75 per cent (25 per cent of these being social recoveries only). There were no relapses within 3 months of treatment. These results compare favourably with cardiazol therapy. The initial intravenous dose of picrotoxin was 4 c.cm. of a solution containing 3 mg. per c.cm. The rate of injection is unimportant. If this dose was subconvulsant, 3 days later a dose increased by 1 c.cm. was given. The maximal dosage required was 11 c.cm. The greatest number of injections given was 22 and the smallest 9. With picrotoxin, multiple convulsions follow-

ing one injection are common, 2 being usual and 4 the maximum. The interval between the injection and the first convulsion varies between 5 and 40 minutes, the average being about 20 minutes. An intramuscular injection of seconal (a barbiturate) after the second convulsion will prevent further convulsions. A steady rise in pulse-rate or systolic pressure after injection indicates that a convulsion is likely to follow. The convulsion produced by picrotoxin is practically identical with that produced by cardiazol. It is initiated by a cry or cough followed by a spasmodic opening of the mouth. The initial clonic phase lasts about 6 seconds; this is followed by a tonic phase of 12 to 14 seconds, then a final clonic phase of about 40 seconds. The cyanosis, flush, and post-paroxysmal motor agitation resemble those of cardiazol. No patients showed any intense fear of treatment. All those who had also been subjected to a cardiazol course preferred picrotoxin. The only complications were dislocation of the jaw and shoulder and one fracture of the left scapula.

Insulin Shock Therapy

The effect of insulin treatment on 33 schizophrenic patients is discussed by P. G. Reynolds. The dosage used to produce coma varied from 1 to 440 units. Among the patients who showed good remissions, the average maximal dose was 227 units, while among those who showed little or no improvement it was 199 units. Psychotherapeutic approach was made easier in some cases by the development of intense psychomotor excitement, this being considered of favourable prognostic significance as it is never exhibited by deteriorated patients. Its occurrence, however, renders abrupt termination of the hypoglycaemia essential. A milder and more prolonged form of excitement was also encountered, characterized *inter alia* by slurred speech, hilarious euphoria, and erotic behaviour. When coma is prolonged it is sometimes necessary to give intravenous injections of glucose and intramuscular injections of adrenaline solution, in addition to the usual glucose by mouth or nasal tube. Neurological and urticarial sequelae sometimes result. Supplementary treatment with cardiazol is indicated when patients are insulin resistant. Favourable results were obtained in 80 per cent of cases with a history of less than 6 months' duration.

S. Lups published 3 cases of schizophrenia, treated with the insulin method of Sakel, in which a paradoxical phenomenon was observed. After the administration of sugar by the nasal route in the course of the insulin-coma, the patients did not rouse from their coma but became more deeply comatose. In 2 cases, the coma underwent a modification as the patients recovered, and they lost consciousness only after feeding. Coma was protracted in all 3 cases. Adrenaline was of no avail in terminating the state; only intravenous glucose was effective.

Circulatory changes. —E. Messinger endeavoured to collect data regarding the changes in the circulatory system during prolonged insulin hypoglycaemic treatment such as the Sakel insulin 'shock' regime for schizophrenia. It was found that peripheral vasomotor phenomena and cardio-aortic dilatation of the aortic bulb and ascending aorta appeared quite regularly during the course of treatment, and persisted in some cases for weeks or months. These cardiovascular changes were considered physiological rather than pathological. X-ray studies confirmed these findings and demonstrated a relatively greater increase in the basal than in the apical diameters of the heart. The electrocardiographic findings were also recorded, consisting mainly of flattening and inversion of T waves and sinus arrhythmias.

Blood changes. — With a view to determining the level of serum potassium and serum calcium, blood examinations were made by J. L. Clegg in 4 patients of schizophrenic type who were all receiving insulin shock therapy. The estimations were carried out before the morning injection of insulin and just before the interruption of coma. It was found that the K/Ca ratio and the potassium level tended to fall during coma, while the calcium figure remained steady. The 'resting' potassium fluctuated, but always remained above normal, while the 'resting' calcium, though seldom varying, was also above normal in some cases.

Histamine Phosphate

W. Marshall and J. S. Tarwater put forward the hypothesis that various psychological conditions may be produced by allergic factors which cause abnormal cerebral reactions. They treated a group of mentally ill patients, including schizophrenics, manic depressives, and catatonics. One group was placed on 5 per cent peptone solution administered subcutaneously in graded doses. The initial injection was 0.3 c.cm. twice a week; this was increased by 0.2 c.cm. until a maximal dosage of 1.5 c.cm. was attained. The other groups were treated with 0.1 c.cm. of a 1 in 1,000

solution of histamine phosphate increased every other day by 0.1 c.cm. until 1 c.cm. had been given. Eighteen patients benefited from the histamine therapy, which the authors suggested acted as a form of mild shock. The mode of action is analogous to that of insulin shock therapy as used in the treatment of schizophrenia.

Results of Shock and Convulsion Therapy

S. W. Gillman and D. N. Parfitt reported the results, which were very disappointing, of 34 schizophrenics by cardiazol, and contested von Meduna's rationale for this treatment i.e. that schizophrenia and epilepsy were antagonistic and rarely combined in the same patient, on the grounds that the association of epilepsy and melancholia was rarer, that schizophrenics did not improve when epilepsy developed, and that the seizures of chronic schizophrenia were not due to vasovagal syncope but were sometimes typical major fits. The percentage of patients who developed hypoglycaemic fits from insulin was 73 as opposed to the usually quoted figure of 30 to 45. They might occur before, during, or after coma, the third type being uncommon. Schizophrenics with a short history did well and chronic cases badly, irrespective of fits, and speaking generally fits were rather unimportant incidents except that they occasionally accelerated recovery when it might reasonably have been expected. The conclusions reached were (i) that any antagonism between schizophrenia and epilepsy was very far from proved, (ii) that hypoglycaemic fits induced by insulin did not have any influence on the ultimate prognosis of schizophrenia, and (iii) that this was also true with regard to cardiazol.

H. H. Reese reviewed the results of hypoglycaemia and convulsive therapy in schizophrenia. The literature shows a variation of between 50 and 85 per cent of remissions in cases of one year's duration when treated with insulin. The optimal number of recoveries in an untreated group is only 30 per cent. The remissions from insulin therapy are of good quality, the patient's insight being keener and his emotional state improved. Reese gave an initial dose of 60 units, with a daily increase of 10 to 30 units, until a shock dose of 70 to 240 units had been given. The shock should not be continued for more than 2½ to 3 hours, and the period of hypoglycaemia should not exceed 6 hours. The patient should be kept warm and the air passages clear during the period of shock. Cardiazol can be used to produce a convulsion but it may also induce a sense of fear. Reese considers that all cases of schizophrenia should be given insulin therapy first. In stuporous, depressed, or catatonic states, cardiazol may be given. If one method fails, the other should be tried. Insulin on the whole shows better results than metrazol (cardiazol) in the treatment of schizophrenia. Early paranoid and agitated catatonic patients respond best to insulin, and stuporous catatonic and depressed hebephrenic patients respond best to cardiazol. Insulin treatment should be given for a minimum of 60 days or 90 days in older disease.

H. Stalker *et al.* compared the results of treatment by ordinary hospital methods, hypoglycaemia, and convulsant drugs in 218 cases of schizophrenia. They found that there was no numerical difference in the results of treatment in the 3 groups. Paranoid cases gave the best results with hypoglycaemia and states of stupor while psychoneurotics who had been resistant to psychotherapy furnished the best results with convulsant therapy. Treatment with convulsant drugs and insulin reduced the average length of stay in hospital. Spontaneous remissions occurred in certain cases and were found to be most likely in cases in which affect is well preserved and the harmonious relations between mood and thought is little if at all disturbed.

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Clegg, J. L. (1939) *Lancet*, **1**, 871

Denyssen, J. A. F., and Watterson, D. J. (1938) *J. ment. Sci.*, **84**, 1002.

Dick, A., and McAdam, W. (1938) *J. ment. Sci.*, **84**, 999

Dynes, J. B., and Tod, H. (1939) *J. ment. Sci.*, **85**, 796

Gillman, S. W., and Parfitt, D. N. (1938) *Lancet*, **2**, 663

Guttman, E., and Reitmann, F. (1939) *J. ment. Sci.*, **85**, 789

Hamsa, W. R., and Bennett, A. L. (1939) *J. Amer. med. Ass.*, **112**, 2244

Hayman, M., and Brody, M. W. (1939) *J. Amer. med. Ass.*, **112**, 310.

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- Lups, S. (1939) *Klin. Wschr.*, **18**, 813.
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 Napier, F. J. (1939) *J. ment. Sci.*, **85**, 802.
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 Struppler, T., and Struppler, V. (1939) *Klin. Wschr.*, **18**, 749.
 Valko, J. (1939) *Klin. Wschr.*, **18**, 915.
 Walk, A., and Mayer-Gross, W. (1938) *J. ment. Sci.*, **84**, 637.

PSYCHOSES: TOXIC INFECTIVE PSYCHOSES

See also Vol. X, p. 316

Bromide Intoxication

Wuth in 1927 published an exact method of estimating the amount of bromides in blood. Toxic symptoms may be expected if 25 to 35 per cent of the total halogens are replaced by bromides; replacement of 40 per cent is usually considered to be fatal. Epileptics appear to have a greater tolerance than others for bromides. The chief symptoms of bromide intoxication are mental torpor, acne, coated tongue, emaciation, digestive disorders, impotence or menstrual disturbances, sluggish pupillary reactions, slurred speech, unsteady gait, tremors of the tongue and fingers, and reflex changes. The most common type of bromide psychosis is delirium, which usually lasts 3 to 6 weeks. Cases of bromide hallucinosis and of Korsakow's syndrome have been observed. A mortality up to 11.7 per cent has been recorded. A report of 50 cases of bromide psychosis is given by F. J. Curran, 33 patients had delirious reaction, one suffered from bromide hallucinosis, and one woman from obsessive neurosis for 10 years. Most of these patients used bromides following alcoholism. In some patients the bromide psychosis was superimposed on other mental diseases. Treatment consists in stopping the drug, giving sodium chloride by mouth or intravenously, forcing fluids, and controlling the stage of excitement. Bromides are eliminated very slowly, they accumulate rapidly even when doses of 45 to 60 gr. are given daily, delirium may occur within a few weeks, even from ordinary therapeutic doses. The author thinks that appropriate legislation should be secured to restrict the sale of bromides.

Curran, F. J. (1938) *J. nerv. ment. Dis.*, **88**, 163.

PSYCHOSES: ALCOHOLIC PSYCHOSES

See also Vol. X, p. 332

Types and Aetiology

L. Minski has made a study of 50 patients admitted to a mental hospital on account of various conditions resulting from alcoholic excess. Of these 31 were males and 19 females, the social and intellectual level of the men was quite high, and their occupations included that of stockbroker, architect, accountant, and schoolmaster. Of the 50, 31 were psychopaths, 7 manic-depressives, 5 reactive depressives, 4 mentally defectives, 2 suffered from obsessions, and one from epilepsy. The largest number of patients belonged to a group of constitutional psychopathic inferiors. The history of the psychopaths suggested difficulties in childhood and in their early home environment. They resorted to alcohol as a means of escape from their trouble. Other reasons given were the presence of insomnia or pain; the result of an accident, and a feeling of social inferiority. Another group considered that the environment was at fault. Although these patients did quite well in hospital, they relapsed soon after discharge. The prognosis was thought to be definitely bad, their condition resulting from environmental factors rather than 'alcoholic heredity'. There was no evidence to support the Freudian view that homosexuality was the cause of chronic alcoholism. The author considers that patients admitted to mental hospitals and labelled

'alcoholic' present the same symptoms and signs, apart from the constitutional factors, as patients suffering from the same diseases caused by other toxic agents.

Minski, L. (1938) *J. ment. Sci.*, **84**, 985.

Korsakow's Syndrome

Treatment

E. N. Rowlands and J. F. Wilkinson stated that the most striking therapeutic results with vitamin B₁ have been obtained in alcoholic neuritis. Moreover, the patients can be cured in spite of continuing the intake of alcohol. There is considerable evidence supporting the view that this condition is attributable to lack of vitamin B₁ rather than a specific toxic action, e.g. alcohol does not hasten the onset of beri-beri and actually delays the onset of symptoms of polyneuritis in rats. They report a marked improvement in a case of Korsakow's psychosis both in the neurological and mental condition. They found that gross deficiencies of vitamin B₁ were present in alcoholic neuritis, and partial deficiencies in simple achlorhydric anaemia.

Rowlands, E. N., and Wilkinson, J. F. (1938) *Brit. med. J.*, **2**, 878.

PSYCHOSES: PRE-SENILE AND SENILE PSYCHOSES

See also Vol. X, p. 342

Pick's Disease

K. Lowenberg *et al.* described a case of Pick's disease which was unusual in that it appeared in early adult life with definite hereditary features. The patient's mother died at 28 of an illness characterized by gross mental deterioration, with convulsions, convulsive seizures, and loss of vision, a very similar illness to that of the patient. Numerous members of the family of both mother and father suffered from alcoholism, psychopathic personality, mental deficiency, and psychoses. The patient was quite normal until 21, when he had an attack of confusion and restlessness which terminated in convulsions. In the next 4 years he showed a steadily progressive intellectual deterioration. On examination at the age of 25, an encephalogram showed frontal atrophy and internal and external hydrocephalus. Biopsy showed fat-laden glitter cells, proliferation of microglia and macroglia, and myelin fragmentation. Mentally he showed gross impairment of attention, perception, and memory. His aphasia was variable and his answers usually bore some resemblance to the stimulus object. He showed perseveration and apparently senseless word-association. Social deterioration was severe but variable. In mood he was apathetic or mildly euphoric. The next 2 years witnessed a progressive physical and mental decline, culminating in complete and mute helplessness, a diffuse spasticity with diminished reflexes and contractures, and death. This patient is the youngest case of Pick's disease so far recorded. The usual range of the time of onset is between 45 and 70.

I. C. Nichols and W. C. Weigner state that, in Pick's disease, the individual's ability to use memory in the formation of new ideational material is disturbed. This is brought out by careful psychological study. In addition, psychological examination also reveals frontal lobe symptoms, such as psychical inertia, stereotypy, and disturbances of general and of ethical judgement. On encephalographic examination, circumscribed atrophy may be seen, enlargement of the ventricles, and pools of subarachnoid air overlying the atrophic areas. The course is progressive, leading to a relatively early death. At autopsy strikingly circumscribed areas of atrophy will be observed, chiefly in the frontal, temporal, and insular areas. On microscopical examination severe diminution of cells is seen, intense gliosis, the presence of Pick's cells containing argentophil bodies, but very few senile plaques and very little Alzheimer's fibrillary degeneration. As other diseases have also been named 'Pick's disease', it was suggested that the name 'idiopathic circumscribed pre-senile cerebral atrophy' should be given to this affection.

Lowenberg, K., Boyd, D. A., Jr., and Salton, D. D. (1939) *Arch. Neurol. Psychiat., Chicago*, **41**, 1004.

Nichols, I. C., and Weigner, W. C. (1939) *Brain*, **61**, 237.

PUERPERIUM

See also Vol. X, p. 365, Cumulative Supplement, Key Nos. 1326-1329, and p. 31 of this volume

Complications other than Sepsis*Insanity*

H. Bruce Williams gave a résumé of some mental and nervous conditions which may accompany pregnancy, the puerperium, or the lactation period. The puerperal group was by far the largest and almost entirely represented by psychoses of functional origin, whereas the psychoses of pregnancy were more likely to have an organic origin. Except in the toxic group the obstetrical experience probably acted only as a precipitating factor to hasten the appearance of a mental derangement which would inevitably have become obvious at some period of life under conditions of unusual stress. Termination of pregnancy, however desirable from the social and eugenic points of view, did not play any part in the treatment of the pregnant insane woman and there was not any medical justification or legal right for abortion. But an attack of puerperal insanity within 3 years, or a history of 2 previous attacks, was an indication for abortion.

Williams, H. B. (1938) *Med. J. Aust.*, **2**, 677

Puerperal Sepsis*Prophylaxis*

R. Cruickshank and G. E. Godber, after investigating 6 cases of puerperal sepsis in the maternity ward of a general hospital and examples of streptococcal infection among children in diphtheria wards, concluded that infection might be spread by the air-borne route, and that routine nursing methods to limit such infection were often insufficient. To counteract such spread, the wards should be freely ventilated, particularly in the winter months, when the risks of spread were greatest, and damp dusting and sweeping, with a liberal use of soap and water should be carried out. A slightly more troublesome and more costly precaution was spraying the air and surfaces with aerosols. Patients with a vaginal or cervical discharge contaminated by the streptococcus might be as dangerous carriers as those with respiratory infections. After diphtheria and measles liability to streptococcal infection was increased, additional factors likely to encourage this condition should be checked by examination of new cases so as to exclude those with tonsillitis or otitis media; in such cases nasal swabs should be taken because half the contacts were nasal and not faecal carriers. Neither the meningococcus nor the pertussis organism had more than a very limited viability in the atmosphere.

Sulphonamide drugs.—From experiments on mice E. D. Hoare found that streptococcal infection was controlled by M & B 693 and sulphanilamide, and that uninfected women after receiving sulphanilamide 0.5 g. or M & B 693 1.5 g., three times a day, showed a much higher bactericidal power of the blood. The administration of these drugs was therefore recommended as a prophylactic measure in maternity cases and some surgical cases when there was a risk of haemolytic streptococcal infection. The suggested dose was 1 g. of either drug thrice daily, starting with the onset of labour and continued for 3 or 4 days.

Clostridium welchii Infection

Treatment with sulphanilamide. J. F. Sadusk and C. P. Manahan considered that puerperal infections due to *Clostridium welchii* occurred more often in post-abortion conditions than after delivery at full term. Mortality is extremely high, and 60 to 75 per cent of the total mortality was found in post-abortion cases. The possibility that this organism may normally be found in the lower portion of the human vagina is being investigated. Two cases were reported in which the infection was successfully treated with sulphanilamide. In the first case a therapeutic abortion was induced and blood and uterine contents collected at the operation were positive for *Cl. welchii*. Although the patient was critically ill oral administration of sulphanilamide was started, giving divided doses every 4 hours; the total daily dosages were 5.7, 6.0, 7.2, 4.8, 4.2, and 2.4 g. The blood culture was sterile on the second day. By the eighth day the temperature was normal. The vaginal cultures showed continued

presence of *Cl. welchii* up to the seventh day of treatment. In the second case, following spontaneous abortion, sulphanilamide therapy was equally successful. In cases in which severe infection was present and late diagnosis made, massive doses of sulphanilamide, at least 6 to 8 g. daily, should be given in conjunction with specific antiserum, and accurate determinations of the sulphanilamide concentration in the blood made daily. Experiments *in vitro* showed that the action of sulphanilamide on *Cl. welchii* was bacteriostatic and not bactericidal.

Cruickshank, R., and Godber, G. E. (1939) *Lancet*, **1**, 741

Hoare, I. D. (1939) *Lancet*, **1**, 76.

Sadusk, J. F., and Manahan, C. P. (1939) *J. Amer. med. Ass.*, **113**, 14.

Inhibition of Lactation

Oestrin

G. L. Foss and P. Phillips reported their results in the suppression of lactation in cases in which this was desirable, such as still-birth, miscarriage, death of the child, disease or illness of the mother (tuberculosis, heart disease, eclampsia). The treatment was by the oral administration of oestrin, the preparation used being progynon, each dragée containing 1,000 international units of oestrone. When the treatment was first started 2 doses of 5 dragées were given daily for 2 to 6 days. Subsequently, in order to keep up a continuous supply of the inhibiting hormone, 5 doses of 2 dragées each were given 2-hourly throughout the day; some patients received one dragée hourly during the day and, if awake, during the night. The treatment should begin soon after delivery with 2 doses of 5 dragées each on the first day, followed by 5 doses of 2 dragées 2-hourly on the second or more days if necessary. When the treatment was begun later it might be necessary to continue a dosage of 2 dragées 2-hourly for 2 to 4 days. The average total dosage was 20 to 30 dragées. In 26 cases 5 dragées twice in one day were sufficient, and in 21 cases 5 dragées twice daily for 2 or 3 days were enough. In 62 cases this treatment was quite satisfactory, and older methods, such as restricted fluid, purgation, and belladonna plasters, were unnecessary. At a later period of lactation, mammary abscess reacted favourably to this treatment. It was concluded that oestrone acted, not by inhibition of the anterior pituitary, but on the mammae, by preventing in some way the action of the anterior pituitary, possibly by directly antagonizing it.

Foss, G. L., and Phillips, P. (1938) *Brit. med. J.*, **2**, 887

PYELITIS

See also Vol. X, p. 404; Cumulative Supplement, Key Nos. 1330, 1332, and p. 159 of this volume.

Pyelitis

Actiology and Pathology

H. F. Dietrich reported 4 cases of pyuria in female children due to dysentery bacilli, which were presumed to have reached the urinary tract by the same path as *Bact. coli*. There was not any evidence of haemic infection, and the sex of the children supported the view of an ascending infection. None of the patients had a previous history of dysentery and there were no distinguishing clinical features of the disease.

Treatment

Sulphanilamide.—H. I. Helmholtz compared the effect as urinary antiseptics of organic acids and sulphonamide preparations. On account of the ease with which they can be given by the mouth and the freedom from gastric irritation by sulphonamide preparations, the average case should be treated in this way. This is particularly so in acute cases, when the urine is alkaline, and in proteus infections. On the other hand sulphanilamide has not any action on *Streptococcus faecalis*. The organic acid and the sulphanilamide treatments, the first in an acid and the other best in an alkaline urine, supplement each other.

Adrenal cortex and bone marrow.—M. Wahl published a case of very severe pyelonephritis which he treated by the injection of a mixture of adrenal cortex and of bone marrow. This method was used a few times with considerable success in the treatment of *coli* bacillosis and in typhoid fever and in the author's case of pyelonephritis the result was quick and astonishingly complete. There was no retention

during the height of the infective condition and the injection was tolerated very well. The patient was relieved of his disease within 3 days.

Dietrich, H. F. (1938) *Amer. J. Dis. Child.*, **56**, 270

Helmholz, H. F. (1938) *Acta Paediatr., Stockh.*, **23**, 1.

Wahl, M. (1939) *J. Urol. méd. chir.*, **47**, 359

Pyelitis of Pregnancy

Morbid Anatomy

S R Woodruff and A H Milbert examined 60 consecutive normal pregnancies by excretory urography, employing 20 c cm. of diodrast. Progressive dilatation of the upper part of the urinary tract, more marked on the right side, with redundancy and lateral displacement of the ureters, was present in most cases. Special attention to renal mobility in pregnancy showed that pre-existing nephroptosis was partially corrected during pregnancy but was exaggerated once the mechanical support of the gravid uterus was removed. Such abnormal mobility favoured obstruction by angulation of the ureter. The dilatation of the ureters and renal pelvis in pregnancy were regarded as chiefly due to mechanical factors, and deprecated the use of the terms 'pyelitis of pregnancy' and 'hydronephrosis of pregnancy'. In the former an infection had been engrafted on some lesion, usually obstructive. Hydronephrosis of pregnancy represented an obstructive uropathy, transient and physiological, which returned to normal after delivery. Most pregnant women without previous obstructive lesions pass through gestation uneventfully, whereas those who experience difficulty have a condition which antedated gestation.

Woodruff, S R., and Milbert, A H (1938) *J. Amer. med. Ass.*, **111**, 1607

PYLORIC OBSTRUCTION

See also Vol X, p 426

Hypertrophic Stenosis of the Pylorus

Actiology

I A Cockayne published 4 new pedigrees showing the occurrence of congenital pyloric stenosis in first and second cousins. These pedigrees, together with others previously published, contained 4 instances in which a man transmitted the condition to his son, thus proving that the condition is not determined by a single sex-linked gene recessive or incompletely dominant, but the possibility that it was determined by a sex-linked gene acting with an autosomal dominant gene was not excluded.

Treatment

K H Tallerman analysed 102 cases of hypertrophic pyloric stenosis coming under observation during 10 years. In 94 per cent the tumour was palpable, 4 were treated medically, with one death. Rammstedt's operation was performed in 98 cases with 14 deaths, 4 of which were regarded as surgical fatalities and of the remaining 10, 7 succumbed to gastro-enteritis subsequent to operation. Of the recoveries 56 had symptoms for less than 3 weeks before admission to hospital and in 7 cases symptoms had been present for 5 weeks or longer. Of the fatal cases, 6 had shown symptoms for less than 3 weeks and 3 for more than 5 weeks. The longest duration of symptoms was 8 weeks in the case of a child who recovered. The short time spent in hospital by most of the infants treated surgically contrasted with the long periods usually required for medical treatment. Pyloric stenosis, when the symptoms have persisted for some time, should not be regarded as a true surgical emergency, but should undergo a short period of preliminary medical treatment, to counteract the accompanying dehydration, alkalosis, and gastritis. In older infants, first seen when about 3 months of age, and when in relatively good condition, medical rather than surgical treatment was especially indicated, since it is generally recognized that after this age the condition is likely to improve spontaneously and eventually to subside. Of the 4 medically treated patients mentioned above, 2 were 3 months old and responded well. Only 2 of those operated upon had reached the age of 3 months on admission.

Eumydrin.—R. H. Dodds reported the results of the treatment of congenital stenosis of the pylorus by eumydrin (atropine methylnitrate) which had a similar

systemic effect to that of atropine, but was 50 times less toxic and half as powerful as an antispasmodic. This treatment had been described in 61 cases by E. Svensgaard. Dodds reported 20 cases thus treated; 16 were cured, one proved fatal while treated by eumydrin, and in 3 the treatment failed and these were successfully operated upon. When infants were admitted they were first given one fluid drachm of barium sulphate cream in one fluid ounce of milk and radiograms taken every 8 to 12 hours; meanwhile isotonic saline to which 5 per cent dextrose was often added, was given subcutaneously to relieve dehydration and alkalosis due to vomiting. This must be carried out before the administration of eumydrin is begun. Eumydrin, which was readily soluble in water, was given in gradually increasing doses, from 1 to 4 or 6 c cm. of 1 in 10,000 of eumydrin 20 minutes before meals. Transient flushing in one infant after taking 8 c cm. of the solution was the only atropine-like toxic effect noticed. The treatment was threefold: (i) of dehydration and alkalosis, due to vomiting (ii) relief of the pyloric obstruction, either by surgical operation which produced its object immediately, or by eumydrin which had a gradual effect, and (iii) prevention of infection to which the patients were particularly prone.

H. Vertue reported the successful treatment of 21 cases of congenital pyloric stenosis by eumydrin in doses of 0.25 mg. in water half an hour before 5 feeds in the 24 hours. After 48 hours' treatment the vomiting diminished, the loss of weight was arrested, pain was less, and sleep and contentment followed.

Cockayne, E. A. (1938) *Arch. Dis. Childh.*, **13**, 249

Dodds, R. H. (1939) *Lancet*, **1**, 12

Svensgaard, E. (1935) *Arch. Dis. Childh.*, **10**, 443

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PYREXIA OF OBSCURE ORIGIN

See also Vol. X, p. 440.

Neurogenic Hyperthermia

T. C. Erickson discussed neurogenic hyperthermia in which the rectal temperature rises rapidly, the trunk is relatively warm, but the extremities are icy and dry. The patient is almost always unconscious. Hyperpnoea is usually observed, and tachycardia is characteristic. Neurogenic hyperthermia was frequently observed following operations on the pituitary fossa, the region of the third ventricle, or the posterior fossa as well as after head injuries. Body temperature is affected by the heart, the general circulation, the general metabolism, cutaneous vasoconstriction and vasodilatation, and the respiration. The manifestations of neurogenic hyperthermia may therefore vary according to which portions of the neural centres and pathways are concerned in its production. Neurogenic hyperthermia may be prevented or at least alleviated by close attention to the patient's rectal temperature in relation to his thermal environment. As therapeutic agents, transfusion is often indicated and should be performed in the early stage. Tepid sponges, ice water enemas, and ice bags are recommended. Repeated small doses of morphine, $\frac{1}{4}$ or $\frac{1}{2}$ gr., were often useful.

W. Griesel discussed central fever which, in contrast to infectious fever, means increased temperature resulting from alteration in the central nervous system. In a case of central fever there are no signs of infection and therefore no leucocytosis, the patient may not feel much malaise in spite of a high temperature. In healthy people and patients affected by an infectious disease the skin temperature and the temperature measured per rectum did not differ very much, usually not more than 2° C. In a case of central fever the skin temperature is independent of the rectal temperature. When, however, the heart and blood circulation were much impaired in a case of infectious fever, the difference between the skin and rectal temperatures was observed. This difference is a valuable sign in patients treated by fever therapy, being an early indication of weakness in the heart and circulatory system. A marked difference indicates the necessity for stimulating the heart and circulation and for terminating fever therapy. Regular examination of skin and rectal temperature should therefore be made in such a case. By simultaneous examination of both

temperatures central fever was demonstrated in a patient who, in consequence of meningitis, had developed an infective fever.

Erickson, T. C. (1939) *Brain*, **62**, 172.

Griesel, W. (1939) *Dtsch. Z. Nervenheilk.*, **148**, 159.

RADIOLOGY IN DIAGNOSIS AND TREATMENT

See also Vol. X, p 456, and pp 18 and 23 of this volume

Contrast Media

Thorium Dioxide

R. M. Stuck and D. L. Reeves studied the effect of thorotrast in dogs, cats, and monkeys when given by spinal, cisternal, and ventricular injection. Prolonged storage of thorotrast in the tissues produces first mild and then later intense fibrosis, which in white rats has been followed by sarcoma. Its pathological effects are due to 3 causes: the particulate nature of the colloidal suspension, the great weight of thorium which is the second heaviest metal, and its radio-activity. The thorotrast is picked up and stored by the reticulo-endothelial cells and its great weight causes it to fall to the bottom of cavities such as the subarachnoid space. The resulting fibrosis frequently leads to hydrocephalus. In view of this and of the fact that it may damage the cranial nerves, the clinical applications of thorotrast to ventriculography and encephalography are extremely dangerous.

D. C. Collins discussed the danger of using thorium dioxide solution in mammography unless immediate surgical removal of the breast was performed. Even careful lavage of the ducts with saline could not be relied upon to remove this substance. Thorium dioxide, which in a 25 per cent solution was known as thorotrast, broke down into mesothorium and radiothorium, and it was considered by Taft that the burning alpha rays which it emitted were about 10,000 times as toxic to human tissues as the therapeutic gamma rays of radium. The author quoted 2 cases in which mammography was performed, with the help of thorium dioxide solution, after the observation in one case of multiple nodules in the left breast and in the other of a solitary nodule near the right nipple. Operation was not performed at the time of examination, but within 6 months new tumour-like formations appeared, resembling carcinoma. Radiographs revealed a considerable quantity of thorium dioxide still present in both breasts. Amputation was performed in each case, and a diagnosis of marked foreign-body reaction was confirmed, but the impression that malignancy would in time probably have supervened received confirmation.

W. Loehr discussed whether the tendency to bleed was increased by thorotrast used for arteriography. The author's experience as well as reports given by other neurosurgeons and the result of animal experiments indicate that it is not. Post-operative haemorrhage results from special conditions in the patient, such as injured respiratory function after an accident and technical errors. A special disposition for bleeding is a rare exception.

Sodium Monoiodomethanesulphonate

Because of the results of irritation, such as encysted masses in the peritoneal cavity leading to local peritonitis, which have occurred after the use of iodized poppy-seed oil, P. Titus *et al.* experimented to find a radio-opaque substance which was not irritating and could be injected into the uterus in order to help in diagnosis. For nearly 2 years they had used a compound consisting of sodium monoiodomethanesulphonate (skiodan), which contained 52 per cent of iodine in stable combination; to 40 per cent of this substance there was added acacia 20 per cent to increase viscosity. This compound did not liberate free iodine and was rapidly excreted in the urine. The X-ray pictures were more distinct than those obtained with iodized poppy-seed oil. It was suggested that this substance might be extremely useful in bronchoscopy.

Collins, D. C. (1939) *Canad. med. Ass. J.*, **40**, 440.

Loehr, W. (1939) *Zbl. Neuroch.*, **4**, 65.

Stuck, R. M., and Reeves, D. L. (1938) *Arch. Neurol. Psychiat.*, Chicago, **40**, 86.

Titus, P., Tafel, R. E., McClellan, R. H., and Messer, F. C. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 889.

Systematic Radio-Diagnosis

Bronchography

J. Gosselin and J. E. Perron describe a successful method of bronchography which is simple to perform and which causes no untoward reaction in the patient. The lipiodol (iodized oil) is introduced through a small auricular speculum in one nostril. A small rubber tube is attached to the speculum to avoid irritation of the mucous membrane. The patient may lie or sit, leaning to left or right according to the side it is desired to demonstrate. Through the speculum are introduced 3 doses, at 5-minute intervals, of 5 c.cm. of an anaesthetic solution containing cocaine hydrochloride 1 g., potassium sulphite 0.3 g., phenol 0.1 g., 1 in 1,000 adrenaline solution 5 g., cherry-laurel water 20 g., and distilled water 95 g., followed, after another 5 minutes' interval, by the lipiodol. The tongue is pulled out at each introduction of the solution to avoid the swallowing reflex. Speed in taking the necessary X-rays is important as only 4 or 5 minutes are available before expectoration commences. Out of 100 cases, only 5 or 6 had to be re-examined owing to lack of a good result. Contra-indications are acute or ulcerative tuberculosis, recent haemoptysis, or iodine idiosyncrasy.

Tomography

H. Roche discussed the value of tomography in tuberculosis of the lungs, in determining the exact position and size of cavities it was a great advance on ordinary X-ray examination. It might indicate the institution or cessation of an artificial pneumothorax. It had been valuable in thoracic surgery (i) in the planning of thoracoplasties to conserve as much healthy lung as possible, (ii) in the radiological exploration of the contralateral lung before and after treatment, and (iii) in the post-operative control of the operated lung in cases of thoracoplasty and external pneumolysis. Tomography was of great value in the analysis of root shadows, with its use enlarged hilar shadows should always be accurately diagnosed.

Arteriography

E. Mackh claimed that thorotrast for arteriography was harmless and that the thorium was injected in such small quantity that dangerous irritation of tissues and tumour formation did not result. Thorotrast was not retained, so that sudden death, sometimes observed after injection of thorotrast, was not a result of the injection. This method of examination is not suitable for a tumour outside the cerebral hemisphere. If ventriculography and arteriography are compared for diagnostic value, arteriography is stated usually to be better tolerated. Arteriography was more valuable for examination if the side of the cerebrum affected was known. Indication for arteriography was given for determining the site and character of a tumour in the cerebral hemispheres. Arteriography was of special value for tumours in the temporal lobe as well as for those cases in which on ventriculography the ventricles did not show a sufficient quantity of air. At the place where the anterior cerebral artery was observed in a normal brain, a region bare of vessels was seen in a case of frontal-lobe tumour. Diagnosis often was very difficult in the case of a tumour in the anterior fossa of the skull, because of the great variability in the vessels in that site. A tumour in the occipital lobe sometimes showed no definite evidence either by arteriography or by ventriculography. In cases of malignant glioma, the calibre of the vessels was often abnormally large and often vessels were observed in an abnormal position. With temporal lobe tumours special difficulty arose in diagnosis of the special nature of a tumour because there are few vessels in that region, so that typical alterations in vessels were often not observed. In such a case, however, the middle cerebral artery was nearly always displaced upwards and a form of 'siphon of the carotid artery' was abnormal.

The number of vessels was increased in the neighbourhood of the falx cerebri in cases of meningiomas in a parasagittal situation. Meningiomas in the temporal lobe were often observed in a place supplied by few vessels only. Usually arteriography did not enable the differential diagnosis to be made with regard to other benign tumours. The main point is that practically every case of malignant glioma may be diagnosed or excluded.

Encephalography

M. Weinbren discussed a method of encephalography with small quantities of air, introduced by Laruelle, which did not pretend to replace routine encephalography or

ventriculography but rather to act as a first line of investigation. Its simplicity recommended its use in cases of head injuries and epilepsy, and it could be performed as an out-patient procedure. The technique employed amounted to nothing more than a lumbar puncture which was carried out with the patient in the erect position. About 10 c.cm. of cerebrospinal fluid were drawn off slowly and 5 c.cm. of air then injected through the lumbar puncture. A radiograph was taken 3 to 5 minutes after the injection, the patient being kept in position and the needle not withdrawn until the film had been developed. If the result was unsatisfactory a further 3 to 5 c.cm. of air might be injected and another film taken. The method was based on the assumption that normally the 3 superior ventricles are placed in relation to the sagittal plane with mathematical accuracy, and that any pathological condition would disturb the relationship of one of them in relation to the various base-lines, and any distortion of the symmetry of the ventricular system would indicate a morbid condition.

Ventriculography

A technique for radiography of the fourth ventricle is described by T. Garratt Hardman. This fulfils the necessary requirements, i.e. the visualization of the fourth ventricle if it is not occluded and if the cerebral aqueduct (of Sylvius) is patent. If the method is reliable, failure to demonstrate this portion of the ventricular system will be of definite diagnostic value in cases of internal hydrocephalus. The fourth ventricle is only visible when the aqueduct is dilated and the third ventricle larger than normal. The part to be demonstrated must be uppermost but the positions adopted in the past were not successful in filling the fourth ventricle. The recommended posture is the ordinary nose-forehead position, with the head resting on a small pillow and the base line of the skull at an angle of 90° with the table. Interpretations of X-ray appearances of films taken in the lateral position are given as follows: (i) A well-filled aqueduct and fourth ventricle, without deformity or displacement, indicates an obstruction of the foramina of Magendie and Luschka, which may be due to arachnoiditis or to a congenital deformity of the cerebellum. (ii) Filling defects or inroads upon the shadow of the fourth ventricle may be due to tumours of the floor or roof of the ventricle, or to extrinsic tumours of the vermis, pons, or cerebellar hemispheres. As these tumours become larger they will probably cause a forward displacement of the aqueduct and, finally, complete occlusion. (iii) A block of the aqueduct may be due to inflammatory ependymitis and is said to produce a funnel-shaped stricture. It is differentiated from a tumour by the absence of displacement. (iv) A pineal tumour may produce a characteristic defect and obliteration of the supra-pineal recess.

Myelography

Myelography with the aid of lipiodol or other contrast media, such as thorotrast, is somewhat dangerous. I. Lindgren reports that in some cases good visibility in myelography resulted from injection of air into the cerebrospinal canal. This method was valuable in a case of an expanding lesion invading the subarachnoidal space. Arachnoid adhesions, however, and membranes not causing a marked obstruction can be demonstrated only by a positive contrast-medium. If, after evacuation of the cerebrospinal fluid and injection of air, myelography does not give a clear result, myelography using lipiodol must be delayed for a week because a deceptive block of the contrast-medium may be produced in a space not sufficiently filled by cerebrospinal fluid.

The Contrast Cystogram

S. McMahon emphasized the value of the contrast cystogram in the diagnosis of multiple diverticula of the bladder and suggested a method which prevented an excessive amount of air being forced into the bladder, thus rendering the procedure unsafe. A urethral catheter is passed through the urethra and strapped at the meatus. The bladder is completely emptied and the first X-ray exposure taken. Next, a tube and funnel are filled with warm 5 per cent sodium iodide solution and, with the funnel held 15 to 18 inches above, the solution is allowed to run slowly into the bladder. A second cystogram is then taken. The tube and funnel are disconnected and the solution is allowed to flow out into a glass measuring-jar. A second jar and funnel should have been prepared. This is now attached to the catheter which has remained *in situ* and an amount of water equal to the opaque solution drawn off is put into the second jar. This causes an equivalent amount of air to be passed through the catheter into the bladder. The third X-ray is then taken and the catheter disconnected.

It is claimed that by using this method the danger of introducing an excessive amount of air is obviated.

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Mackh, E. (1939) *Dtsch. Z. Chir.*, **252**, 145.

McMahon, S. (1939) *Brit. J. Urol.*, **11**, 133.

Roche, H. (1938) *Brit. J. Tuberc.*, **32**, 236.

Weinbren, M. (1938) *Brit. J. Radiol.*, N.S. **11**, 705.

Radiotherapy

Lobar Pneumonia and Broncho-Pneumonia

F. V. Powell has treated by X-rays 231 patients with acute lobar and broncho-pneumonia whose ages varied between 2 and 70. Of these only 16 have died, giving a mortality-rate of 7 per cent. The technique consists of giving 250 to 350 r, using 135 kV and a 3 mm. aluminium filter. A 40 cm. skin-target distance is used. As soon as a diagnosis is made, and without waiting for typing, treatment is given anteriorly or posteriorly over an area a little larger than the involved portion of lung. If the temperature has not returned to normal within 36 hours a further treatment of 200 r is given over the opposite skin area. In some cases the temperature falls within 12 hours of the first treatment. The only contra-indication is a definite leucopenia such as is present in some cases of post-influenzal pneumonia. Broncho-pneumonia seems more variable in its response to irradiation than the lobar type.

Radon Gas in Skin Lesions

A. Tidinow used radon gas dissolved in melted petroleum jelly and allowed to cool at 40 °C. in Cellophane envelopes for the treatment of skin lesions. In this way, soft and pliable radio-active plaques were produced, filling well the contours of the body. Telangiectases were very rare and burns did not occur. Congenital naevi which did not blanch readily were treated with some success. Sometimes 3 applications, each lasting 3 days, at 3-monthly intervals were needed. A full erythema reaction appeared 2 to 3 weeks after application. Ultra-violet rays help to avoid telangiectases. A single 3-day dose of radio-active ointment containing 0.5 mc. of radon per c.cm. of ointment is usually enough to cure sycosis barbae. Warts, single and multiple, flat plantar warts, and callosities have responded well to 12-hour doses. The treatment of hypertrichosis was difficult as heavy dosage was needed to destroy the deep hair follicles. The best results were obtained where disfiguring hair had grown excessively in later life. Radon ointment and plaques must be treated as radium by workers and kept in metal boxes when not in use.

Granulomas

R. McWhirter divided cases of granulomas under discussion into 3 groups: actinomycosis; anal and vulvar granulomas; and granulomas of unknown origin.

In the first class the lesions appeared on the face and neck, the abdomen, the chest wall, and the buttock. Daily irradiations of 100 r were given over a prolonged period, the total dosages being as high as 4,000 r. Daily treatment was superior to weekly treatment and a hard quality beam was advised. In 12 out of 15 cases the sinuses completely healed; in the remaining 3 there was marked improvement. The second group resulted from long-standing gonorrhoeal infection. The lesions were very radio-sensitive, and sometimes it was only necessary to give one single dose of 300 r. Seven cases were successfully treated (see Fig. 21). One of the more extensive cases was 3 months pregnant at the time and was subsequently delivered of a normal full-time child. The third group consisted of lesions involving the mouth, pharynx, and neck. The causal organism was not detected, but the clinical history and appearance suggested that the condition was produced by a fungous infection. There was a resemblance to malignancy but the characteristic induration was lacking. These patients were in poor health, they responded very well to daily doses of 100 r continued over a month, but subsequently deteriorated and died.

Skin Injuries

E. Uhlmann discusses his method of treating skin injuries resulting from irradiation by the use of X-rays. Radium emanations are directed on to white or yellow vaseline. It has been demonstrated that vaseline will absorb 9 times as much radium emanation as

tion as a similar volume of air and 36 times as much as water at room temperature. The concentration amounts to 50 to 100 electrostatic units per gram of vaseline. This radon ointment has a half-value period of nearly 4 days, and it is applied to the affected area. The dressing is left in place for 8 hours, then removed, and repeated

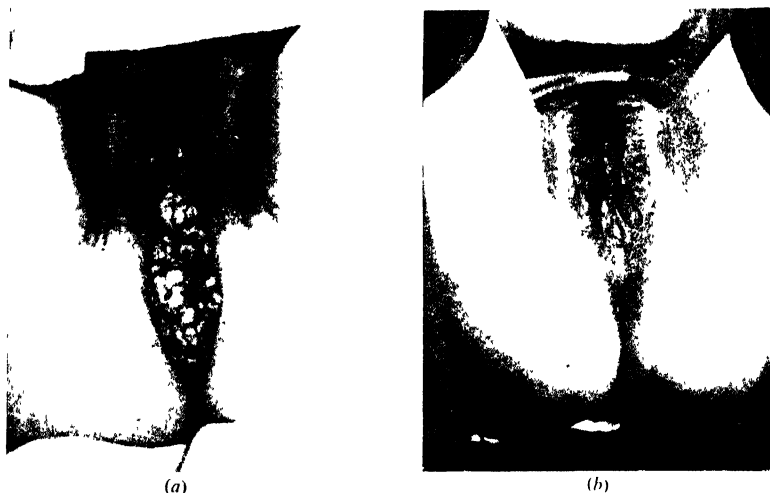


FIG. 21 - Anal and vulvar granulomas. (a) before X-ray treatment (29/1/36) (b) after X-ray treatment (16/3/36) (From *British Journal of Radiology*, 1938)

at weekly intervals. The author maintains that, as the injuries are caused by roentgen rays and by gamma rays, the alpha rays used in his treatment have a counter-active effect. In the interval the skin is best covered by 10 per cent boric-beryllium ointment. Of the 70 cases treated by the author only 2 failed to obtain complete cure, and in these the lesion was found to have undergone malignant changes.

Effect on Healing of Wounds

W. G. H. Dobbs investigated the effect of X-rays on the healing of wounds which had been induced in albino rats. The rays used were produced by a full wave, mechanically rectified generator at a tension of 95 Kv (peak). With a Coolidge tube, 4 ma. of current, 40 cm. focal skin distance, and no added filter, the output measured in air was 60 roentgens per minute. Irradiation with 300 *r* immediately after operation significantly increased the tensile strength of wounds as compared with the controls, but exposure to higher dosage 1,020 *r* and 1,800 *r* immediately after operation, and 1,800 *r* one and 3 weeks before operation, showed that the wounds revealed a definite decrease in tensile strength. Irradiation with 1,800 *r*, 24 hours after operation, showed no significant decrease. Increased tensile strength does not necessarily imply stimulation of fibroplasia or other known processes concerned with healing.

Inflammatory Conditions

H. Wintz and R. Reding discussed the indications and the use of radiotherapy in inflammatory conditions. It should be tried in all cases in which other methods fail, and certain inflammatory conditions, e.g. mammary abscesses, carbuncles, infected glands, and adnexitis, heal better and more quickly by irradiation than by any other means. Radiotherapy lowers the blood pressure and causes a vagotonic excitation followed by sympathetic stimulation. Leucopenia constantly develops after roentgen therapy. The doses vary with the organ or part of the body involved.

F. O. Coe advocates the routine treatment by X-rays of certain inflammatory conditions, e.g. puerperal and acute mastitis, furuncles and carbuncles, erysipelas, lobar and broncho-pneumonia and pneumonias with delayed resolution, cervical adenitis, and sinusitis. In the last-named condition the technique used is 100 to 120 *r* at 112,000 volts through 5 mm. aluminium to each area, the entire treatment being given 6 times. The successful treatment of this condition is considered to be of particular interest in view of the high incidence amongst children of sinus disease.

All the author's cases of cervical adenitis are now treated by X-ray therapy on account of its unqualified success. Dosage is 100 to 160 *r* at 112,000 volts through 3 mm. aluminium; 3 treatments are given. X-ray therapy is considered a safe and valuable agent in the management of inflammatory conditions, only small doses being necessary.

Carbuncles and Furuncles

H. Wintz advocates X-ray therapy as an alternative to surgical treatment in dealing with such infections as carbuncles, and large boils on the lips. Forty per cent of the 'skin unit' dose is advocated in the treatment of inflammatory conditions of the breast. Such dosage stops lactation, and the inflammatory process thus becomes self-limiting. In parametritis 25 per cent of the skin unit dose, applied to the centre of the pelvis, meets with favourable response.

Endocrine Glands

S. Bray reported 7 cases of rash as occurring during and after the irradiation treatment of endocrine glands. In these cases treatment was directed on the ovaries, thyroid, or pituitary. The condition was first noticed in 1930 after protracted fractional treatment of ovary and thyroid cases by X-rays excited at a voltage of 196 Kv and filtered through 2 mm. copper and 1 mm. aluminium. With the use of still heavier filters the condition has been noticed more frequently.

The rash was described as irritating, red, and papular, and it was confined chiefly to the thighs, trunk, and upper arms. None of the observed cases showed vesication or scarring. In each case the rash cleared in a few days, the irritation being allayed by calamine and menthol. There was no recurrence, even when further X-ray treatment was given. It is suggested that the rash was caused by the effect of short X-rays on one of the components of the endocrine system.

Resistance of Ovarian Tissue

The extraordinary resistance of ovarian tissue to radiation is discussed by H. W. Jacob. He describes the interesting case of a nurse of 37, whose menstrual periods were accompanied by metastatic abscesses throughout the body and especially on the arm at the site of an old injury from the breaking of a hypodermic needle. Temporary castration was produced by X-rays and neither periods nor abscesses appeared for 8 months. Simultaneous return of both conditions occurred at the end of this time. A cystic ovary had been removed prior to the injury which produced the abscesses. A permanent sterilizing dose was next applied, the ovary receiving approximately 700 *r*. After 8 months, menstruation and abscesses again returned. A further dose of 1,200 *r* to the ovary failed to produce permanent sterilization, and surgical intervention had to take the form of a panhysterectomy and left salpingo-oophorectomy.

Chaoul Technique

E. P. Pendergrass *et al.* enumerate the outstanding features of the Chaoul method of X-ray therapy which consists of the use of low voltages (45 to 60 Kv), direct contact with the patient's skin, and an anti-cathode the gold-plated nickel target of which acts as both target and filter. The total dose per field is not arbitrarily selected but depends almost entirely upon the reactions of the treated area. The authors state as their experience that the daily dose per field varied from 100 to 400 *r* (*r* measured in air, without back-scatter). The Chaoul technique is recommended in the treatment of lesions the site of which makes short treatments desirable, and in lesions in which it is desirable to obtain the maximal effect in superficial tissues. The cases treated by the authors include such conditions as warts, angiomas, keloids, nasal catarrh, pruritus ani, rectal condylomas, and skin carcinomas.

E. W. Frecker holds the view that the biological effect of all X-rays and of radiations from radium are of the same nature but differ in wave-length. The idea that γ radiation possesses any intrinsic biological value is dismissed. The effective penetration of rays from the Chaoul tube at 5 cm. distance exceeds that of the average radium application. The applicator must be brought in actual contact with the lesion. By this unique method it is maintained that the irradiation is chiefly confined to the abnormal tissues and therefore efficient dosage may be given without undue regard to the normal tissue. Further, the depth dosage being only 50 per cent at 1.5 cm. the underlying tissues retain their viability and power of regeneration. Description is given of the apparatus used, with suggested dosage, and case reports are appended of a facial basal-celled carcinoma, metastatic nodules on the anterior

surface of the thorax, papilloma of the external urethral meatus, and leucoplakia of the vulva, all of which were successfully treated by the Chaoul method.

In superficial carcinoma.—M. I. Karlin reported on the use of Chaoul's method of contact irradiation of superficial carcinomas with X-rays. In his view this method is well able to replace radium therapy in cancers of the lip and tongue, and certain cutaneous growths. A daily dose of 200–500 *r* are given and the total dose is between 5,000 and 10,000 *r*. The tube is placed about 5 cm. (2 inches) from the tumour. The author described a few clinical histories and, by showing many photographs taken before, during, and after irradiation was able to prove the efficacy of the method.

Following the Chaoul technique, a method of treating superficial cancer by X-ray caustic is described by G. J. Van der Plaats. The only essential apparatus for per-



FIG. 22.—Extensive carcinoma of left upper eyelid, (a) before and (b) after treatment by Van der Plaats' method (From *British Journal of Radiology*, 1939)

forming this treatment is a normal shock-proof X-ray tube for superficial therapy, allowing the use of a small focal skin distance. The author has used a special tube for contact and endotherapy. The surface dose of radiation is considered of no importance, the ultimate aim being to direct the maximal amount on to the base of the tumour, but to save the underlying tissues in which the process of regeneration must begin. By using the tube, steeper depth-dose curves may be obtained, thus giving a space selectivity which though detrimental to tumour cells is harmless to healthy tissue. The author used contact therapy with 50 Kv constant tension, 0.2 mm. of aluminium total filtration, and 2 cm. focal skin distance, the dose being applied at one sitting. (See Fig. 22)

Grenz Rays

In skin diseases.—H. Jungmann reviews the uses of Grenz rays in various skin diseases and advocates their application in (i) lupus vulgaris, (ii) chronic eczematous affections of the scalp or near the eyes or genital organs, (iii) Darier's disease, (iv) localized scleroderma, (v) lupus pernio, (vi) pruritus ani et vulvae, and (vii) sycosis barbae. Grenz rays are X-rays of a very long wave-length, between 1 and 3 A.U., and produced by a tension of from 5 to 12 Kv. They are easily filtered by air and are generally considered safer than X-rays for the treatment of skin conditions. It is suggested that trial should be made of them, and only if this proves unsatisfactory should X-rays be used. Contra-indications are psoriasis and squamous-cell epitheliomas. In other clinical conditions, such as acne and alopecia, judgement must be reserved.

In eye diseases.—R. L. Pfeiffer treated diseases of the eye with Grenz rays. These rays produce erythema, and in larger doses, pain in the skin, but Pfeiffer did not find that these reactions occurred in the conjunctiva which he considered more tolerant. Untoward reactions were not experienced even with high doses of the rays, which

are much safer than the usual X-rays. Pfeiffer treated over 300 cases of eye disease and found the rays of great use in the treatment of superficial lesions of the eyeball, cornea, bulbar conjunctiva, episclera, and sclera. The treatment is painless and an analgesic effect on the eye was noted. The most striking response was observed in corneal ulcers, and treatment was almost equally dramatic in episcleritis and scleritis. In non-ulcerative keratitis the results were not so consistent and in vascularized keratitis only partial relief was obtained. The effect on dystrophic diseases was not good.

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 — and Reding, R. (1939) *J. Radiol. Electrol.*, **23**, 241.

RAYNAUD'S PHENOMENON

See also Vol. X, p. 486, and Cumulative Supplement, Key No. 1345.

Morbid Anatomy

P. Sunder-Plassmann examined the nervous lesions in Raynaud's phenomenon by Bielschowsky's ammoniacal silver method and found various changes, especially hydropic swelling of the autonomic ganglion cells. He concluded that there is a toxic state of the autonomic nervous system, and that the nervous lesions with local factors, such as cold, precipitate the attacks. Resection of the sympathetic improves the condition but the treatment should be supplemented by administration of thyroid and vitamin B₁.

Sunder-Plassmann, P. (1938) *Dtsch. Z. Chir.*, **251**, 125.

Treatment

Intravenous Papaverine

M. G. Mulinos *et al.* treated Raynaud's disease with intravenous injections of papaverine. Presuming that the condition of the fingers is produced by spasm of the digital artery in response to cold, they treated the patients with antispasmodics. Amyl nitrite was used but was discarded as being too dangerous in its general effect of lowering the blood pressure. Histamine hydrochloride given by iontophoresis dilated the minute vessels but increased arterial spasm. They therefore combined this treatment with the intravenous injection of papaverine hydrochloride 60 to 120 mg., 3 times a week for a period of 8 to 12 weeks. The immediate effect was to raise the blood pressure and to increase the rate of blood flow in the hands. The cyanosis and pain of the extremities were relieved and the trophic lesions healed.

Parathyroidectomy

Intraperitoneal injections of parathyroid extract produce scleroderma in young rats. This observation led A. R. Bernheim and J. H. Garlock to perform parathyroidectomy for the scleroderma accompanying Raynaud's disease. They believed that sclerodermatous changes occurred in the skin because the vessels in Raynaud's disease are constricted and the blood supply to the part interfered with. In their cases there was no change in the blood calcium but the blood phosphorus was raised. They reported results of 17 cases. If the Raynaud's disease was not accompanied by

scleroderma, the condition improved immediately after operation but the improvement was not maintained. Improvement occurred in all cases of scleroderma and relapse was only witnessed in one. In some of the cases the maximal improvement did not appear until some months after the operation. The operation must be performed in the early stages before articular changes and contractures have developed. The authors do not advocate the operation for Raynaud's phenomenon alone and think that the immediate improvement in some of these cases may have been due to the unintentional division of the sympathetic in the neck whilst operating on the parathyroid gland. When these fibres regenerated, the symptoms of Raynaud's disease returned.

Bernheim, A. R., and Garlock, J. H. (1939) *Arch. Surg., Chicago*, **38**, 543.

Mulinos, M. G., Shulman, I., and Mufson, I. (1939) *Amer. J. med. Sci.*, **197**, 793.

RECTUM DISEASES

See also Vol. X, p. 502, and Cumulative Supplement, Key Nos. 1346-1356.

Endometriosis

L. Bazy *et al.* reported a case of rectal endometrioma, a small uterine deposit occurring in the rectal mucosa. This localization is very rare and the symptoms are those of dysentery. Endoscopic examination at different times during the period enabled detection of the condition, the haemorrhages occurred shortly before menstruation. The nature of the erosions was also studied by the injection of folliculin, which showed them to be uterine mucosa. Some of these cases are extremely difficult to diagnose; a number pass under the name of rectal neuralgia. Radiotherapy is thought to be effective in rectal endometriosis.

Bazy, I., Blondin, S., and Chêne, P. (1939) *Pr. méd.*, **47**, 785

Carcinoma of Rectum

Diagnosis

C. C. Tucker and C. A. Hellwig emphasize the wide range of possible causes of anal symptoms and the close resemblance between harmless and highly malignant anal lesions. One-third of a series of malignant conditions were discovered by routine histological examination of clinically benign lesions. Routine microscopical examination in proctological practice is thus demonstrated to be of great value.

Treatment

The management of a permanent colostomy was reviewed by I. J. Druckerman. The diet should be calculated to induce constipation and produce a stool which is hard, dry, and small in amount. A bland low-residue diet with high carbohydrate and low-fat content was the most successful. It was unnecessary to limit the quantity of food or fluid taken but the fluid should be taken only at meal-times, because it might excite a gastro-colic reflex. Drugs might be necessary to produce constipation. Bismuth carbonate 15 to 60 gr. 3 times a day, kaolin, opium, or charcoal may be tried. Kerol given in a 3-minim capsule before breakfast deodorizes the excreta. Purgatives should not be employed. Druckerman recommended administration of vitamin concentrates, especially vitamin D, to patients on the constipating diet. Irrigation was necessary in patients who could not obtain a regular action about once in 24 hours. Open irrigation was preferable to closed as it was more thorough, lasting 45 minutes, but closed irrigation was pleasanter and therefore more acceptable to some patients. Colostomy bags were rarely prescribed, and never for left-sided colostomies. They were expensive, difficult to clean, became offensive and musty, led to dermatitis of the surrounding skin, and might cause a ventral hernia by suction. Instead, the exposed intestine was covered with gauze dipped in soft-paraffin or boric ointment; another piece of gauze dressing was applied over this, and a supporting belt worn over the whole. Dermatitis from faecal irritation was difficult to cure and the most efficacious ointment was 10 per cent zinc oxide and 10 per cent finely powdered aluminium in anhydrous lanolin. Stenosis of the colostomy opening was treated with manual or bougie dilatation preferably after the local employment of novocain (procaine hydrochloride). General measures included careful instructions

to the patient concerning this regime, the regulation of exercise so as not to produce an excessively frequent action, and an individual approach to the problem, the placid patient requiring different handling from the patient in whom the presence of a colostomy inspires suicidal thoughts.

Druckerman, L. J. (1938) *Amer. J. digest Dis.*, **5**, 382

Tucker, C. C., and Hellwig, C. A. (1938) *J. Amer. med. Ass.*, **111**, 1270.

REFLEXES IN DIAGNOSIS

See also Vol. X, p. 558.

Reflexes elicited in Shoulder Girdle

F Duensing discusses the idio-reflex, produced by mechanical excitation in the posterior part of the deltoid muscle, in normal persons and in patients affected by a spastic or amyostatic syndrome. Examination by action current corresponded to the result observed in an idio-reflex. Infiltration by novocain (procaine hydrochloride) nearly abolished the deltoid reflex. It was diminished by an affection of the peripheral neurons, and was increased by affection of the pyramidal tract. The biceps reflex produced by a blow on the inferior angle of the scapula completely corresponded to an idio-reflex of the biceps muscle. Probably it is identical with this reflex. Idio-reflex of the biceps therefore may be produced (i) from the biceps tendon, (ii) from the periosteum of the radius, (iii) from scapula to biceps muscle. In a case of hyperactivity of reflexes this reflex will be produced also by excitation of other bones, for example, the clavicle and thorax. The triceps reflex produced by a blow on the acromion, and the infra-spinatus reflex produced by a blow on the medial part of scapula are also idio-reflexes. The last mentioned may be mistaken for the result of direct mechanical excitation of this muscle. Muscular receptors form the starting-point for these idio-reflexes. Receptors probably do not exist in the periosteum. Idio-reflex of muscles from distant parts in a case of spastic paresis probably result from a marked diminution of the threshold of excitation.

Duensing, F. (1939) *Dtsch. Z. Nervenheilk.*, **149**, 45.

The Knee-Jerk

K. J. Franklin described a new method of eliciting the knee-jerk. The patient lies supine on a table with his legs hanging down comfortably over its edge. He then

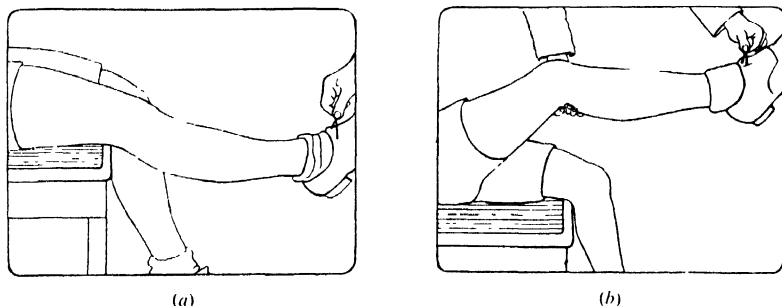


FIG. 23 — (a) Usual initial position for the new knee-jerk test, (b) alternative initial position for the new knee-jerk test (from *The Lancet*, 1938)

takes his mind off what is happening, while the observer raises one leg and holds it horizontal by a grip on the shoe-laces. When this grip is relaxed, the lower leg drops for a short distance before the drop is arrested by a sharp contraction of the extensor muscles of the thigh. After this arrest, the leg often falls farther until it is vertical; but the extent and rate of the further fall vary with the conscious reaction of the patient to the sharp extensor contraction. The response can be tested simultaneously in both legs. 'Re-enforcement' can be applied in the usual manner by getting the patient to clench the hands together. Franklin considers that the advantage of this method is that the stimulus applied is a standard one and that, as the amount of

drop can be measured in degrees from the horizontal, it can serve as a quantitative record.

Franklin, K. J. (1938) *Lancet*, 2, 1287.

Tonic Foot Response to Stimulation of Sole

K. Goldstein described slow tonic plantar flexion and adduction of the toes with hollowing of the sole and wrinkling of its skin resulting from stimulation of the sole in certain cases of brain disease. Increasing stimulation caused an increase of the movement. The posture persisted for some time after cessation of stimulation and then the foot returned slowly to its habitual position. This tonic response is considered to be one of the earlier signs of a lesion of the frontal lobe. It has a special diagnostic value, especially when it appears on the side homolateral to a lesion of the frontal lobe, indicating that the affection of one frontal lobe is pressing upon the other frontal lobe or that the lesion has spread across the middle line. This sign points especially to a lesion of the medial part of the frontal lobe. Like the so-called forced grasping of the hand, it is an expression of an abnormal 'turning to' movement of the organism to the stimulus and appears to be a response of the lower mechanisms when the higher centres, especially of the frontal lobes, are damaged.

Goldstein, K. (1938) *Braun*, 61, 269.

REFRACTION, PRACTICAL METHODS

See also Vol. X, p. 565, and Cumulative Supplement, Key No. 1358

Refraction with Mydriatic

Homatropine and Benzedrine

H. F. Sudranski investigated the effects of a 5 per cent solution of homatropine hydrochloride with a 1 per cent solution of benzedrine sulphate used as a cycloplegic. He found that the drugs acted synergically to produce mydriasis and resulted in a larger pupil. The cycloplegia lasted for only 5 to 8 hours because it was produced by such a small dose of homatropine (1 minim of a 5 per cent solution); this is of great advantage to the patient in the practice of refraction.

Sudranski, H. F. (1938) *Arch. Ophthalmol.*, N.Y., 20, 585

RESUSCITATION

See also Vol. X, p. 596, and Cumulative Supplement, Key No. 1363

Methods of Resuscitation

Mechanical Respiration

U. Blackwell treated 14 cases of poliomyelitis, 6 cases of diaphragmatic paralysis due to diphtheria, and one case of toxic polyneuritis, all exhibiting respiratory distress, by mechanical respiration. Five of the poliomyelitis cases were of the bulbar type and these patients all died. Six of the remainder are alive and progressing well; 3 of these had intercostal paralysis only. Among the diphtheria cases there were 4 deaths and 2 recoveries. The only case of polyneuritis recovered.

Oxygen Administration Apparatus

D. J. Pachman gives a simple comprehensive description of an open-top box, the sides and floor of which are impermeable to air, used for the administration of oxygen to infants and young children. An ice compartment maintains a comfortable temperature and humidity. Diagrams with measurements are included, and the author points out that the advantages of this type of apparatus are: it is inexpensive to make and operate, simple to use, and portable. No motors are required. Children may be fed, examined, and treated without removal. Plexiglas windows allow clear vision from within and without the box. Oxygen concentrations as high as 64 per cent have been obtained, using an inflow of 4 to 5 litres of oxygen per minute. The explanation of the mechanism of this method of oxygen therapy is given as follows. There is a balance between the inflow of oxygen and its diffusion upward, and

oxygen is slightly heavier than air. The results may be due to a combination of these two factors.

Blackwell, U. (1939) *Lancet*, **1**, 1430.

Pachman, D. J. (1938) *J. Pediat.*, **13**, 902.

RETINA DISEASES

See also Vol. X, p. 611, Cumulative Supplement, Key Nos. 1364-1379; and p. 130 of this volume.

Diagnosis

Vital Staining

Basic dyes used for intra-vitam staining for microscopical examination stain the structures of the central nervous system, and therefore the retina, but only when given in toxic doses. To overcome this toxicity A. Sorsby used dyes containing a sulphonic acid radical or rhodamine dyes. He found that the normal retina in animals stained only transiently but that if it were damaged the stain was deeper and more prolonged. In man he gave 20 to 30 c.c. of a 10 per cent solution of Kiton Fast Green V intravenously. He found that the retina in optic atrophy did not stain, that tears were more easily seen in detachment of the retina, and that in one case, in which vision in one eye was 6/60 but the ophthalmological findings were normal, the retina did not stain.

Sorsby, A. (1939) *Brit. J. Ophthalmol.*, **23**, 20.

Retinitis Proliferans

B. A. Klien divided retinitis proliferans into 2 groups: (i) in which the formation of connective tissue precedes the formation of new blood vessels, and (ii) in which the formation of new blood vessels is the primary change. The first type may be located anywhere in the fundus and consists of dense opaque white or grey-white membranes. It includes such conditions as tuberculous retinal periphelebitis, neuro-retinitis papulosa of secondary syphilis, and all injuries of the retinal vessels followed by haemorrhage. In this type exudation or haemorrhage from the retina into the vitreous is the primary event and organization of the extravasation leads to the formation of the bands and membranes. The aetiological factor in the second type is degenerative vascular disease leading to circulatory impairment, with the formation of new compensating anastomotic channels, with or without haemorrhages at first. This type therefore occurs in such conditions as diabetes mellitus, tertiary syphilis, and arteriosclerosis. The lesions appear at or near the optic disc and show many newly-formed blood vessels often having a brush-like arrangement. The connective tissue between the vessels is delicate and semi-transparent.

Klien, B. A. (1938) *Arch. Ophthalmol.*, N.Y., **20**, 427.

Vascular Diseases

Obstruction of Central Retinal Artery

R. W. Danielson and J. C. Long reported a case of retinal arterial occlusion in a girl of 19. Previous ocular examination had not revealed any abnormality. The general health was good except for fatigue. She was in the habit of going to sleep with her fist pressed upon her eye. She complained of defective vision of the right eye of sudden and quite recent onset. The central vision of the eyes was equal, 20/15, but the visual fields showed a marked defect in the upper field of the right eye. In the inferior branch of the central retinal artery there was a yellowish area, directly continuous with the vessel and of the same calibre. The blood in the artery immediately distal to this area was darker in colour, thus suggesting that it was venous. It was concluded that the artery was completely obstructed by an embolic plug; alternatively the authors suggest the possibility of the formation of a local clot resulting from stagnation subsequent to long-continued pressure on the globe but this seemed improbable. Extensive physical and laboratory examinations revealed no other local or general defect. Treatment aimed at driving the obstructing plug to a more peripheral site, and this was effected by the application of firm pressure to the eye-ball coupled with sudden release. Amyl nitrite was administered by inhala-

tion, and the eye-ball was then vigorously massaged. The obstruction suddenly moved far into the periphery, some 5 disc diameters from its original site. Vision improved at once. The patient was re-examined several times for a year, and the fundus appeared to be perfectly normal and the girl was unaware of any visual difficulty.

Danielson, R. W., and Long, J. C. (1938) *Amer. J. Ophthalm.*, **21**, 1264.

Tumours

Glioma Retinae

Treatment.—H. B. Stallard describes a method of keeping radon seeds in apposition to the posterior part of the sclera for the treatment of glioma retinae. The seeds are embedded in a strip of Stent's dental wax previously moulded to the sclera at the desired site. The strip is kept in place by sutures traversing the superficial layers of the sclera in front of and behind the equator. No complications such as irritation or infection occurred.

Stallard, H. B. (1938) *Brit. J. Ophthalm.*, **22**, 604.

RHEUMATIC INFECTION, ACUTE

See also Vol X, p. 639, and p. 135 of this volume.

Aetiology

J. C. Meakins, in connexion with the specific relations of tonsillitis to rheumatic fever, condemned the routine removal of the tonsils in order to prevent attacks or immediately after the development of rheumatic fever. Most authorities now agree that tonsillectomy should only be performed after the acute phase of rheumatic fever has definitely subsided, and then only when there is evidence of tonsillar disease. Rheumatic fever was not fundamentally an arthritic disease, any more than syphilis was a skin disease; but both were systemic with localized lesions in the finer vascular architecture, both affected, although after a different pattern, the cardiac and nervous structures. The aetiology of rheumatic fever was unknown and the numerous hypotheses emphasized this ignorance. Whereas formerly the diagnosis of rheumatic fever mainly depended upon the presence of polyarthritis, it was now generally accepted that mitral stenosis, chorea, and fibroid nodules were of more specific significance and were manifestations of the disease. It was 7 times commoner in urban than in rural school populations. Like tuberculosis, it was also a disease of the poor. It was also familial, and some writers had reported its incidence in from 45 to 70 per cent of families in which rheumatic fever occurred. Though no age was immune, it mainly occurred in childhood, between the ages of 6 and 12. The treatment of rheumatic fever was highly unsatisfactory; salicylates made the disease more bearable but no less deadly, thus lulling both patient and medical attendant into a false sense of security, if it was concluded that the disease had become inactive when the temperature was normal. The best treatment after a cure was, as in tuberculosis, a high vitamin diet (particularly vitamin C), and education of the patient for an 'economic' life within his physical capacities. Rheumatic fever was essentially a disease of the heart and not of the joints, and in the heart the ultimate danger lay.

Meakins, J. C. (1938) *Canad. med. Ass. J.*, **39**, 426.

Treatment

Sulphanilamide

From past observations A. F. Coburn and L. V. Moore found that rheumatic subjects who escaped haemolytic streptococcal infections also escaped rheumatic fever. It was concluded that possibly the prevention of streptococcal respiratory infections might influence the development of rheumatic attacks. From observations on a group of rheumatic subjects, conducted in an institution, it was found that the administration of sulphanilamide after the onset of streptococcal throat infections did not prevent rheumatic recurrences. The successful prophylactic use of sulphanilamide against streptococcal respiratory infection was established by investigation of a group of 80 rheumatic children, 79 escaping infection. They also

escaped clinical evidence of rheumatic fever. Animal experiments showed that the administration of sulphanilamide to guinea-pigs, before or after the induction of streptococcal abscesses, failed to sterilize the lesions, but when used prophylactically, the drug prevented the occurrence of spontaneous infection.

A number of patients were treated with sulphanilamide over a period of 6 months in each year for 2 years by C. B. Thomas and R. France. Every patient had had one or more major attacks of rheumatic fever, the last of which had occurred within 3 years of the commencement of treatment. During the first course the patients received 15 gr. of sulphanilamide daily, and during the second course, 20 gr. daily. On account of the small dosage very few toxic symptoms were observed. In the treated patients no case of acute beta haemolytic streptococcal sore throat occurred, although in a few cases the organism was present in small numbers. During the period of treatment there were no major attacks of rheumatism and only two minor attacks occurred, shortly after the commencement of treatment. One major attack occurred two and a half months after its cessation. In a control group, one patient was sent to hospital with acute beta haemolytic streptococcal infection, 4 patients had 5 major attacks of rheumatic fever, and 2 had minor attacks. The result seems to warrant further investigation on these lines.

Coburn, A. F., and Moore, L. V. (1939) *J. clin. Invest.*, **18**, 147.

Thomas, C. B., and France, R. (1939) *Johns Hopk. Hosp. Bull.*, **64**, 67.

RHINOSPORIDIOSIS

See also Vol. X, p. 655

H. Kaye described rhinosporidiosis of the eye in a boy of 16, who complained of a blood-stained discharge from the right eye and of something protruding between the lids. Two large cock's-comb-like excrescences sprang from the palpebral conjunctiva in the fornices. They were excised and microscopically proved to be rhinosporidiosis. There were no polypi in the nasopharynx. The boy was given 0.5 per cent quinine drops. About 2½ years later the boy returned with a red polypoid swelling on the white of the right eye. Examination with the slit-lamp showed it was a recurrence of the same parasitic infection; the fornices had completely healed without leaving any trace of the operation. The polypus was excised and 2 per cent tartar emetic drops were inserted in the conjunctival sac of the infected eye. Eighteen months later there was not any further recurrence. The mode of infection was not obvious but the violent dust storms in the Transvaal, where the patient lived, may have disseminated the spores. The recurrence was possibly due to a few sporangia remaining dormant in the conjunctival sac for 18 months, and then gaining admission through a fresh area, perhaps by rubbing the eye.

Kaye, H. (1938) *Brit. J. Ophthalm.*, **22**, 449.

RICKETS

See also Vol. X, p. 661, and p. 38 of this volume.

Treatment

Prevention

G. O. Harnapp describes the difficulties of an effective prophylaxis of rickets resulting from neglect by the parents of the directions of the medical attendant owing to financial difficulties of obtaining vitamin preparations or ultra-violet radiation for a period long enough to be effective when small doses are prescribed. He recommended a prophylactic 'single dose' of vitamin D₂ which he gave a good many cases with much benefit. The effective dose is 7.5 mg. of vitamin D₂; even larger amounts will do no harm. The main advantages of the 'single-dose' method of prophylaxis seem to be (i) one dose only is necessary; (ii) it is not necessary to rely upon parents; and (iii) the new method is much more economical than the old ones.

Specific

Actions of vitamin D.—F. Albright *et al.* assert that vitamin D possesses 2 separate actions: (i) it increases the absorption of calcium from the gastro-intestinal tract;



Case of vitamin-resistant rickets. A. Patient, boy, aged 4 years, showing short stature, enlarged epiphyses at wrist, ricketsy rosary, and genu valgum. B. Radiograph of hand of same patient, May 1936. C. Radiograph of same patient, December 1938, after treatment with calciferol, calcium gluconate intramuscular injections of vitamin D, and ultra-violet light treatment. (From *Archives of Disease in Childhood* 1939)

and (ii) it increases the phosphate excretion in the urine. Investigations were carried out in a case of vitamin D resistant rickets, to discover the metabolic effects of A.T. 10 (dihydrotachysterol), and parathyroid extract. It was concluded that A.T. 10 possessed the same functions as vitamin D, but the ratio of the second of these actions to that of the first was much greater with A.T. 10, and that because of this difference A.T. 10 was not antirachitic. In this case A.T. 10 did not cause the marked rise in urinary phosphate excretion which it causes in patients with deficient parathyroid glands. The explanation offered is that the calcium-absorption-increasing properties of this substance lead to a decreased activity of the patient's own parathyroid glands, which in turn lead to a decreased urinary phosphorus excretion. The most striking effect of the parathyroid hormone was to increase the urinary phosphorus excretion.

Citric acid and sodium citrate.—A. T. Shohl and A. M. Butler treated two infants, one a female of 11 months and one a male of 5 months, who were both suffering from infantile rickets, with mixtures of citric acid and sodium citrate. Neither of these cases received vitamin D. Satisfactory results were obtained, and deposition of lime salts was detected on the ninth and fourteenth days of therapy respectively. A gain in weight was recorded in both cases. Daily citrate dosage was calculated as the amount contained in 5 or 6 large oranges. It is considered that this new form of therapy is an aid in the treatment of rickets and may be useful both in cases of vitamin D resistant rickets and also in other calcium and phosphorus metabolic disorders.

Vitamin-Resistant Rickets

Cases of rickets which have failed to respond to treatment with vitamin D have been reported. In these cases the disease remains active until growth has ceased and the clinical and X-ray appearance is one of florid rickets. A. Morton Gill reported 4 cases of this condition in which there were no signs of malnutrition, lack of sunlight, calcium drain, or renal disease. None of them showed any response to the usual methods of therapy such as calcium gluconate, calciferol, or intramuscular injections of vitamin D even if continued for many years (see Plate VII). The blood calcium and phosphorus were normal in these cases, but the blood phosphatase was very high, as is always the case in active rickets. It was suggested that the rickets may be due to failure of the utilization of calcium and phosphorus at the site of bone growth.

Albright, F., Sulkowitch, H. W., and Bloomberg, E. (1939) *J. clin. Invest.*, **18**, 165.

Gill, A. M. (1939) *Arch. Dis. Childh.*, **14**, 50.

Harnapp, G. O. (1938) *Dtsch. med. Wschr.*, **64**, 1835.

Shohl, A. T., and Butler, A. M. (1939) *New Engl. J. Med.*, **220**, 515.

SCARLET FEVER

See also Vol. XI, p. 1, Cumulative Supplement, Key No. 1387; and p. 77 of this volume.

A. L. McLean feels that the classification 'scarlet fever' should be replaced by the more comprehensive term 'streptococcal infections of the throat', and should include not only cases with typical rashes but those many others now termed epidemic sore throat, which are equally infective. The similarity of symptoms of scarlet fever, severe tonsillitis, and epidemic sore throat is emphasized, and the various methods of transmission peculiar to each condition are mentioned.

McLean, A. L. (1939) *Canad. med. Ass. J.*, **40**, 108.

Complications

Jaundice

Wisch observed 2 cases of scarlet fever complicated by jaundice. In both it was established that the patients had no previous liver or gall-bladder disease. The jaundice apparently was of allergic origin. After disappearance of the icterus in one case, a typical scarlet fever rheumatoid syndrome developed. The antigen in both cases was thought to be the scarlet fever toxin, and it was pointed out that the clinical symptoms were rather mild and easily controllable. Jaundice developing in

the first 2 or 3 weeks of scarlet fever does not indicate a malignant course of the disease, as shown by these 2 observations.

Wisch (1939) *Munch. med. Wschr.*, **86**, 808.

Treatment

Immunity and Vaccination

J. A. Kolmer, summarizing a series of immunizing experiments on rabbits, supports the view that scarlet fever is primarily a local infection with haemolytic streptococcus belonging to Group A of Lancefield, capable of producing sufficient erythrotoxin for the induction of the characteristic rash. In infection with streptococci of high toxicity and high invasive power, antitoxic immunity alone may be insufficient to afford protection, and result in the production of scarlet fever among individuals possessing sufficient antitoxic immunity for yielding negative Dick skin reactions. Local infections without the exanthem may occur in infections with streptococcus of low toxicity or in individuals possessing sufficient natural antitoxin or that acquired by vaccination with the toxin to prevent the occurrence of the characteristic rash. These may and usually do escape clinical detection and may constitute foci of infection capable of disseminating the disease. For these reasons it seems desirable, if possible, to engender antibacterial as well as antitoxin immunity by vaccination against the disease with vaccines incorporating not only the toxin or toxins but the streptococcus itself.

Sulphanilamide

W. Sako *et al.* described the use of sulphanilamide in scarlet fever. In 100 cases given large doses, complications of the disease developed in 8 whereas among 100 control cases complications occurred in 41. In general the rate of recovery from the acute toxic phase was not accelerated. The authors confirmed the striking modification of the toxæmia effected by early massive doses of antitoxin contained in human convalescent serum and commercial horse serum, administered intravenously. Five out of 10 boys closely exposed to scarlet fever were not protected by the administration of 20 c cm. of pooled human convalescent serum, whereas the other 5 who received in addition sulphanilamide escaped the disease.

Of Complications

Acute haemolytic streptococcal peritonitis—H. S. Banks discusses the treatment of that form of acute haemolytic streptococcal peritonitis which is non-abdominal in origin. He is opposed to laparotomy, and describes a case of scarlet fever manifesting peritonitis towards the end of the fourth week, in which intramuscular injections of the soluble sodium salt of M & B 693 in 3 days rendered the peritoneal fluid sterile. Later the injections were exchanged for M & B 693 in tablet form. The fluid was subsequently withdrawn by aspiration on 4 occasions and, after a protracted convalescence aided by 2 blood transfusions, the patient's condition returned to normal.

Banks, H. S. (1939) *Lancet*, **1**, 983.

Kolmer, J. A. (1939) *Arch. Pediat.*, **56**, 74.

Sako, W., Dwan, P. F., and Platou, E. S. (1938) *J. Amer. med. Ass.*, **111**, 995.

SCIATICA

See also Vol. XI, p. 26.

Aetiology

Changes in Cerebrospinal Fluid

H. Cordel examined the cerebrospinal fluid in 62 cases of sciatica. Abnormalities were observed in 29 cases. Protein, especially albumin, was increased in 28 cases. The number of cells was increased in 5 cases. The gold-sol curve was abnormal in 18 cases, being shifted to the right in 17 cases and to the left in one. Disturbance in the circulation of the cerebrospinal fluid, together with oedema and increased protein, results from inflammation of the intradural portion of the sciatic nerve roots. If a portion of the roots in contact with arachnoidal tissue becomes inflamed, the number of cells and the amount of protein increases. Alteration in the cerebrospinal fluid will not be observed if only the peripheral portion of the nerve is affected.

Cordel, H. (1939) *Neurvenarzt*, **12**, 243.

Diagnosis

G. A. Rost observed, on rectal examination, marked hyperaesthesia in the region of the seminal vesicle in patients with sciatica. Pain was not felt when the prostate was touched. Examination of the urine showed no signs of inflammation in the prostate. Hyperaesthesia was also found on touching the inner wall of the true pelvis. In such a case hyperaesthesia was supposed to result from neuritis in the nerve plexuses which are connected with these organs. The same kind of hyperaesthesia was present in several cases of lumbago. This sign may be of value for the diagnosis of sciatica, as all the other signs may result from suggestion or malingering.

Rost, G. A. (1939) *Nervenarzt*, **12**, 247.

Treatment

Adhesive Strapping

When back strain is associated with sciatica, F. W. Ilfeld considers that it is probably caused by localized muscle spasm. A new method of strapping with adhesive tape is described, by means of which strain on the tensor fasciae latae, the gluteus maximus, and the piriformis muscle is relieved. The subject rests on the unaffected side with the back towards the examiner. The legs are flexed 30 or 40 degrees, the knees being at a right angle, the affected leg is at 20 or 30 degrees of abduction and 20 or 30 of external rotation. Three layers of adhesive tape are employed. The first layer consists of long strips of 2-inch tape which are placed beginning 8 cm. above the knees and 5 cm. from the middle of the anterior thigh. They are brought upward on the thigh, over the crest of the ilium 5 cm. posterior to the anterior superior iliac spine, and continued on to the back as high up as the twelfth dorsal vertebra. Overlapping longitudinal strips are laid on the thigh, crossing the buttock and sacrum into the lumbar region of the back until the whole of the outer thigh is covered. Transverse pieces of adhesive tape are fastened over the longitudinal strips, and a third layer of tape is placed in a position corresponding to the first longitudinal layer. If there is pain on internal rotation of the leg in the prone position, the patient is considered a fit subject for this treatment. The tape is removed after 5 to 7 days and, if the patient is symptom-free, no other treatment is given.

Ilfeld, F. W. (1939) *New Engl. J. Med.*, **220**, 412.

SCLERODERMIA

See also Vol. XI, p. 37, and Cumulative Supplement, Key No. 1390.

Oedematous Sclerodermia of Hardy

H. L. Arnold, Jr., reviewed the characters, and reported a case, of scleroedema adultorum, which is identical with the oedematous sclerodermia of Hardy, and was first described by Buschke. Sixty cases have been reported, usually following either an acute exanthem or acute infection of the upper respiratory tract. In the case reported by Arnold, tuberculous cervical lymphadenitis preceded the condition. Mastoiditis, parotitis, and nephritis have also been precursors of sclerodermia. It is commoner in women than in men.

Stiffening and hardening of the subcutaneous tissue occur in the back of the neck and spreads over the face, arms, and trunk in a few weeks. The legs are affected only in children, and the feet never. A few cases in which the backs of the hands were involved have been reported. The skin looks oedematous but there is no pitting. Pain is absent and sensation, pigmentation, and sweating are not interfered with. Atrophy does not occur and there are no bone changes.

The disease usually progresses for up to 6 weeks and then regresses, complete return to normal occurring in from 1 to 2 years. The condition must be diagnosed from sclerema neonatorum, oedema neonatorum, and necrosis of the subcutaneous fat, and in adults from dermatomyositis, trichinosis, diffuse sclerodermia, and myxoedema.

Histological examination of the skin shows swelling and separation from one another of the bundles of collagen in the deeper layers of the corium. Many observers have seen 'mucin-like' substance lying between these bundles. The blood vessels are dilated and the nerves thickened, and round-celled infiltration is often found around them. The epidermis is unaffected.

The disease is spontaneously cured, but one authority maintains that this can be hastened by thyroid therapy. Massage, baths, and thyroid have all been used in treatment.

The case reported by Arnold occurred in a 15-year-old girl receiving X-ray treatment for tuberculous glands of the neck. The skin involved was board-like to the touch and included the neck; the face except the eyelids, nose, and lips; the trunk down to the buttocks; and the arms and hands with the exception of the fingers and palms. Histological examination showed the typical picture of scleroedema adultorum. Laboratory examination was normal except that the normal relation of serum albumin to serum globulin was reversed. After 3 months the disease was regressing and the relation of serum albumin to serum globulin was again normal. This phenomenon was also observed by Buschke.

Arnold, H. L., Jr. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 210.

SCURVY

See also Vol. XI, p. 44

Concentration of Ascorbic Acid and Complementary Serum Activity

The fact that a correlation exists between the concentration of ascorbic acid in the blood serum and the complementary activity of the serum itself was found by F. E. Ecker *et al.* to be true not only for guinea-pigs but for human beings. Two cases of human scurvy, showing typical symptoms, were kept on a diet free from vitamin C, and received 100 mg. of crystalline ascorbic acid orally for 2 days. The dosage was then increased to 250, 500, 750, and 1,000 mg. daily for a period of one week. Improvement in clinical symptoms occurred within a week of commencing treatment. The original complement titres were only 0.07 and 0.08 c.cm. of a 1 in 15 serum dilution. The ascorbic acid contents of the serum were negligible.

In each case a parallel rise in ascorbic acid and in complement occurred under treatment. When 1 mg. of ascorbic acid per 100 c.cm. of serum was reached, the complement titre reached its maximum, but the ascorbic acid concentration continued until it was 1.44 mg. and 1.9 mg. per 100 c.cm. in the respective cases. Serums secured from daily bleedings were reactivated. Ascorbic acid showed the best reactivating results, but glutathione SH, potassium cyanide, and hydrogen sulphide all brought about reactivation.

Ecker, F. E., Pillemer, L., Griffiths, J. J., and Schwartz, W. P. (1939)
J. Amer. med. Ass., **112**, 1449.

SENESCENCE AND SENILITY

See also Vol. XI, p. 69.

Clinical Observations on a Group of Twelve Centenarians

In Abkhazia, a district in the Caucasus, Soviet Russia, according to the census of 1926 there were 3,792 men of a great age among one million inhabitants; this is a much greater proportion than in any other place in Europe. An expedition of doctors went there and examined 12 persons, aged from 90 to more than 112, one being 140 years.

General Clinical Picture

I. Basilevich reports that almost all these men had a good memory, clear mind, interest in their surroundings, ability to work, and enjoyed life. But in all of them the skin was atrophic, dry, wrinkled, and parchment-like. The muscles were flabby, with lack of subcutaneous fat. There was atrophy of the alveolar process and of the body of the lower jaw, even in those in whom the teeth were well preserved. In most of the centenarians there was a pronounced kyphosis. Radiography showed in some cases slight arthrosis or osteo-arthritis, but in no case osteoporosis. The lungs were healthy. There was absence of ossification in the costal cartilages, and no calcification of the arteries which, however, were arteriosclerotic. The aorta was slightly dilated and elongated. Not one of the centenarians suffered from angina pectoris. The maximal blood systolic pressure was more than 160 mm. Hg in 3 cases only, being 170, 180, and 200 respectively. Slight increase in the heart shadow was noted.

The second sound, especially of the aorta, was slightly accentuated. Bradycardia was always present. The temperature was 36.2–36.8° C. (97.16–98.24° F.). The sight was good, but the hearing was affected in all cases. In 11 the weight was 52 to 60 kg. The growth of hair was weak and there was usually a bald spot on the head. All the centenarians had always enjoyed good health, and, except for malaria, gonorrhoea, and colds, had had no serious disease.

I. Mizrukhn made observations on these centenarians both in hospital and in their ordinary environment. Most of them were sociable, joyous, changeable, adaptable, capable of establishing good effective contact with the younger people and trying to help in the work of the family as much as they could. Some of them had slight symptoms of general asthenia or of the nervous form of cerebral arteriosclerosis, such as headache, vertigo, fatigue, weakness of memory, and aching of the extremities. Miosis, anisocoria, decrease of the patellar reflexes and absence of the abdominal and cremasteric reflexes were observed in addition to a diminution in the sensitivity to pain, and changes in the motor reflexes, such as tremors and slow walking. Sleep was normal. In 2 cases there was pronounced cerebral arteriosclerosis, and only in one case senile imbecility. The author is of the opinion that senile imbecility and very pronounced cerebral arteriosclerosis are consequences of 'pathological' senility.

Functional State of Cardiovascular System

In their study of the functional state of the cardiovascular system of these centenarians, I. Basilevich and I. Turovez found the following: (i) striking decrease of the size of the heart; (ii) a slight increase of the systolic and arteriovenous variation in the content of oxygen, which indicates some retardation of the blood stream; (iii) an increase in the coefficient of utilization of oxygen, (iv) decrease of the oxygen capacity of the blood, (v) a slight arterial and venous hypoxaemia, and (vi) absence of changes in the pressure of carbon dioxide in the arterial and venous alveolar air. These results show a general weakness of the functional capacity of the cardiovascular system in the centenarians. However, no signs or symptoms of cardiovascular insufficiency were noted. This weakness of the cardiovascular system corresponds to the general debility of all the other organs and systems as a result of senile atrophy. All the centenarians could do some light physical work.

Blood Changes

P. Gragerova investigating their blood found polycythaemia (6,100,000 red blood cells) in one, in 6 the number of erythrocytes ranged between 4 and 4.5 million, and in 5 between 2.84 and 3.6 million. The haemoglobin was between 50 and 89 per cent, and the colour index was 0.63 to 1. The number of reticulocytes corresponded in almost all cases to the lower limits of normal. The number of white blood-cells was between 4,000 and 6,000 per c.mm.; the number of lymphocytes was normal, and that of the polymorphonuclears was decreased. The sedimentation rate was normal in 2 cases; in the other 10 it was much accelerated. Thus there is ground to suppose that the rate of the erythrocyte sedimentation in old persons is progressively increased. The opsonic index (Wright's method) was decreased in several cases, the phagocytic activity of the leucocytes was normal except in one case, and the quantity of blood complement was diminished in 5 cases. The author is of opinion that in old persons the resistance of the organism is lower than in younger persons.

I. Turovez found a considerable decrease of the basal metabolism, indicating the weakness of the oxidizing processes. The biochemical investigation of the blood showed no severe morbid changes which could indicate quantitative changes in the metabolic processes. The investigations showed no abnormality in the sugar, chloride, residual nitrogen, and alkaline reserve of the blood. The ratio of potassium to calcium in the blood was changed, as calcium was predominant. The figures of phosphorus and cholesterol in the blood corresponded to the lowest limits. The changes found in the biochemical constituents of the blood completely corresponded with the general decrease of the metabolic processes typical of the senile period of human life.

Basilevich, I. (1938) *Medichny J.*, **8**, 55.

— and Turovez, I. (1938) *Medichny J.*, **8**, 69.

Gragerova, P. (1938) *Medichny J.*, **8**, 87.

Mizrukhn, I. (1938) *Medichny J.*, **8**, 95.

Turovez, I. (1938) *Medichny J.*, **8**, 77.

SEPTICAEMIA AND BACTERIAEMIA

See also Vol. XI, p. 76, Cumulative Supplement, Key No. 1395, and p. 169 of this volume

Staphylococcal Septicaemia*Treatment*

M & B 693—H. J. Wade describes a case of septicaemia due to *Staphylococcus pyogenes* in a man aged 34 treated with *M & B 693* Uleron, 1 g. 3 times a day, was given for 5 days with no response. After an interval of 4 days, *M & B 693* was given, 1 g. 4 times a day for 8 days. The patient improved during this time, but relapsed after discontinuance of the drug, which was therefore again administered after a 4-day interval (1 g. 3 times a day) for 11 days. In spite of a poor initial clinical condition and a tardy response to the drug in the early stages, the last blood culture, taken 4 days after cessation of treatment, was returned negative after 7 days' incubation, and a complete recovery was made.

Wade, H. J. (1939) *Lancet*, **1**, 756.

Streptococcal Septicaemia*Treatment*

Serum and sulphanilamide—A. L. Sheplar *et al.* reported 30 cases of haemolytic streptococcal infection of the nose, throat, and ear, treated with various types of streptococcal serum. In 15 cases the blood on culture yielded bacteria. Seven of the patients died; 3 of the deaths occurred in cases of meningitis in which organisms were identified in the spinal fluid before treatment with serum began, the authors believed that this stage cannot be controlled by serum therapy; the other 4 deaths occurred in patients with streptococcal bacteraemia. Streptococci were not found in the cerebrospinal fluid of the patient suffering from meningitis who recovered. Other treatment, such as blood transfusions and sulphanilamide, was combined with the serum in some cases. Many cases were advanced and some desperate, yet they were helped by the use of the serum. There are dangers and difficulties in the use of streptococcal serum, and the authors suggest that it might be reserved for cases which cannot be controlled by sulphanilamide. On the other hand, it may prevent surgical intervention or be used post-operatively with good result.

Sheplar, A. E., Spence, J. M., and MacNeal, W. J. (1939) *Arch. Surg., Chicago*, **38**, 206.

Gangrenous Meningococcic Purpura*Treatment*

Serum, sulphanilamide, and vitamin A—R. Poinso *et al.* had under their care a case of gangrenous meningococcic purpura, which is a septicæmic eruption appearing spontaneously in the course of a septicaemia. This rare clinical syndrome occurred in a girl aged 3 years, and, in spite of the alarming general condition, with pyrexia, prostration, and extensive ecchymoses, the child was finally discharged as healed after being treated with vitamin A, sulphanilamide, and serum. Serum therapy, after establishing the meningococcal origin by lumbar puncture, consisted in the injection of polyvalent and monovalent serum intrathecally, intramuscularly, and subcutaneously, in doses of 80 c cm., 230 c cm., and 310 c cm. respectively. About 28 gr. of a sulphanilamide compound were at first administered daily, the dosage decreasing to 3 gr. daily, over a period of about a fortnight; the total dose was 15 g. Vitamin A paste was applied locally to the extensive gluteal gangrene, and an ampoule of vitamin A was injected on alternate days.

Poinso, R., Ciaudo, P., Aubanel, J., and Balmann, A. de (1939) *Bull. Soc. méd. Hôp. Paris*, **55**, 891.

SEX HORMONES

See also Vol. XI, p. 90, Cumulative Supplement, Key Nos. 1396–1398; and p. 108 of this volume.

Method of Administration

Subcutaneous Implantation of Pellets

R. Deanesly and A. S. Parkes followed up their earlier account (1937) of a new method of obtaining a prolonged supply of a hormone when administered to animals by a description of the technique used in connexion with the prolonged effect of crystalline gonadal hormones—oestrone, oestradiol, diethylstilboestrol, progesterone, testosterone, and testosterone propionate. The crystalline hormones were compressed into tablets and inserted under the skin of animals (guinea-pigs, rats, mice) when anaesthetized by ether, and pressed into the subcutaneous tissues. An advantage of the tablets over loose crystals was that the amount of hormone absorbed could be more easily estimated, by weighing before insertion and after removal. There was not any serious local reaction, but a capsule of connective tissue eventually formed round the tablet. The tablets were either recovered at a second operation or at necropsy and were dried and re-weighed. The absorption of oestrone from tablets up to 100 mg. amounted to between 2.5 and 50 per cent each month, that of testosterone propionate to about 15 per cent per month, and of testosterone to about 25 per cent. Stilboestrol was absorbed more rapidly than oestrone. The absorption of progesterone tablets was rapid. Other experiments proved that the rate of absorption in rats is only half of that in mice. To increase intensity of action, the insertion of a number of tablets, of a size necessary to last for the desired period, was more effective than the use of one very large tablet, the weight of which was the same as their combined total weight.

After Deanesly and Parkes' earlier report, P. M. I. Bishop recorded the first clinical application of this method in England: a girl aged 20 underwent double ovariectomy for cysts, and soon afterwards suffered from menopausal flushing, and was treated by oestrone, and finally it was found that these symptoms were relieved by an implanted 14 mg. tablet of oestrone for about 4 weeks. Attention was directed to uterine haemorrhage and headache as possible effects of the treatment.

Bishop, P. M. I. (1938) *Brit. med. J.*, **1**, 934.

Deanesly, R., and Parkes, A. S. (1937) *Proc. Roy. Soc.*, B, **123**, 441.

— (1938) *Lancet*, **2**, 606.

Gonadotrophic Substances

Serum Response to Large Doses

Production of 'immune-body' To determine the serum response of patients to injections of large amounts of the gonadotrophic hormone in pregnancy urine, W. Saphin *et al.* investigated the reactions of 9 cryptorchid children and 3 adults. No antagonodotrophic factor was found in the serum of these patients. Antuitrin-S injected into the patients gave rise to a factor in the serum which fixed complement in the presence of the antuitrin-S antigen. The anti-substance was thermolabile, and was probably an immune-body, although some workers had classed it as an antihormone.

Effect of A.P.L. Factor on Human Spermatogenesis

H. S. Rubinstein investigated the effect of the anterior pituitary-like hormone (A.P.L. factor) on human spermatogenesis. Six healthy adult males were studied, 2 preliminary sperm counts being carried out, the semen was collected one day after the previous ejaculation, and for the other 6 to 7 days thereafter, because it was found that after an ejaculation the sperm count increased for the next 6 to 7 days, when it became practically constant. The subjects were then given 3 intramuscular injections of the water-soluble fraction of pregnancy urine weekly, beginning with 100 R.U. The dosage was quickly increased to 300 and 400 R.U. so that, after 2 weeks, a total of 1,000 R.U. per week was given. These injections were given for from 5 to 9 weeks, and weekly specimens of semen were studied. The morphology, viability, and motility of the spermatozoa were unchanged by the injections. In all cases the total count was increased after 4 to 7 weeks' treatment. The figure remained

high in all but one case, and, after the injections ceased, persisted at this level for between 2 and 5 weeks even in the case which had suffered a momentary drop during treatment.

Effect of A.P.L. Factor on Gastric Acidity

H. Felson and L. Schiff endeavoured to discover the effect of anterior pituitary-like hormone on gastric acidity. Four patients and 3 controls were selected for study; of these 3 were males and 4 females. A control period of observation was instituted prior to treatment. Normal acidity was present in only 3 of the subjects. Daily injections of 1 c.cm. antuitrin-S were given subcutaneously, and a total of 195 analyses was made. The results of the authors' experiments lead them to believe that the subcutaneous administration of anterior pituitary-like hormone, in daily doses of 1 c.cm. for a total varying between 30 and 150 injections, produced no constant effect upon the acidity of the gastric secretion comparable with that obtained one hour after the subcutaneous administration of histamine.

Clinical Uses

In peptic ulcer.— D. J. Sandweiss *et al.*, discussing the frequency of active peptic ulcer during pregnancy, found that out of 70,310 consecutive admissions to hospital only one case of active peptic ulcer was found. Other gastro-intestinal disorders such as appendicitis or cholecystitis were not so rare. The effect of pregnancy on an existing ulcer was beneficial. The sex incidence was investigated between the ages of one and 12 years, and was found to be in the ratio of 1 : 1, as against the adult incidence of 4 or 5 male cases to every one female. In a group of 30 women with peptic ulcer, there was a high incidence of deficient function of the anterior lobe of the pituitary, of the thyroid, and of the gonads. It appeared that there might be some endocrine imbalance during the active ulcer stage. It was found that ulcer symptoms were frequently initiated or aggravated by the menopause. The reproductive function did not seem to be impaired by the presence of a peptic ulcer. Treatment with antuitrin-S (anterior pituitary-like hormone), with which the body is 'flooded' during pregnancy, was not thought to be more beneficial in cases of peptic ulcer than other parenteral preparations, but only small doses (200 to 500 rat units daily as compared with 75,000 to 100,000 units excreted daily in the urine during pregnancy) were used.

Production of ovulation.— By intravenous injection of a purified gonadotrophic hormone derived from the serum of pregnant mares, M. L. Davis and A. K. Koff produced, for the first time, ovulation in women. The subjects were all about to be subjected to laparotomy for various pathological conditions, and it was therefore possible to examine the ovaries *in situ* at varying intervals after the injections. Evidence of recent ovulation, based on the histological examination of a corpus luteum, was present in half the patients. The hormone resembled extracts of the anterior pituitary biologically, but differed chemically and biologically from all other known gonadotrophic substances. Clinically it should be efficacious in the treatment of patients in whom growth of the follicle and ovulation are at fault.

Davis, M. E., and Koff, A. K. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 183.

Felson, H., and Schiff, L. (1939) *Amer. J. digest. Dis.*, **5**, 777.

Rubinstein, H. S. (1938) *Endocrinology*, **23**, 75.

Sandweiss, D. J., Saltzstein, H. C., and Farbman, A. A. (1939) *Amer. J. digest. Dis.*, **6**, 6.

Saphir, W., Howell, K. M., and Kunstadter, R. H. (1939) *Endocrinology*, **24**, 182.

Oestrogenic Substances.

Estimation in Blood of Pregnant Women

A method of estimating the free and combined oestrogens in the blood of pregnant women was described by O. Muhlbock. He examined retroplacental blood from healthy women in child-birth and the blood of women with pregnancy toxæmia on whom venesection had been carried out. The blood was collected in a bottle containing alcohol; the alcohol was evaporated and the residue extracted directly by warming with benzene, first in the neutral state and then after addition of hydrochloric acid. Neutral extraction gives the free hormone; extraction after addition of acid gives the combined hormone. In all the blood samples examined from pregnant women, part of the oestrogenic hormone was present in a combined form; this

combined part totalled 30 to 50 per cent. of the biological activity. In order to obtain the total oestrogenic hormone activity in the blood of pregnant women, it was necessary to examine the blood after hydrolysis.

Effect on Structure of Endometrium

From a series of 1,000 endometrial biopsies L. Wilson and R. Kurzrok described 5 in which the structure of the endometrium did not conform to the usual cyclical variations. It was characterized by the presence of cystic glands in association with secreting glands, or decidual-like stroma cells, or both. Its appearance was confined to ovulatory cycles with excessive action of oestrin during the follicular phase which was sometimes delayed. This 'mixed' endometrial change was brought about in a woman with normal menses by prolonging the follicular phase by the administration of oestrin. The attempt to produce it by giving progesterone during anovulatory cycles was unsuccessful owing to endometrial desquamation. This mixed type of endometrium showed that the endometrium was an accurate index of the different phases of ovarian function.

Effect on Gastric Acidity

The possibility of a relation between sex hormones and gastric secretion led L. Schiff *et al.* to investigate the use of theelin in 12 males and 8 females, with special regard to the possible production of achlorhydria. The dosage varied between 3,000 and 10,000 units, and the duration of treatment between 15 and 167 days. Prior to treatment 2 or more gastric analyses had been performed, and, after institution of treatment analyses were made at intervals of one or two weeks; a total of 308 gastric analyses was made. In 11 cases there was no change in the average acidity, in 3 an increase was noted, and in 6 others a decrease. It was not considered that the administration of theelin had any effect on gastric acidity, as demonstrated by these results.

Toxicity of Stilboestrol

J. Varangot reported on the present state of our knowledge regarding the toxicity and oestrogenic activity of stilboestrol. Patients suffering from the menopausal syndrome did well on a daily dose of 1 to 2 mg. for 15 days; trophic changes necessitated a higher dose. The therapeutic activity of stilboestrol was undoubted. Further observations, however, proved that the toxicity of the product was equally constant, the therapeutic dose being toxic, and that the ingestion of the minimal therapeutic dose gave rise to toxic symptoms such as nausea, vomiting, epigastric pain, and anorexia; toxic phenomena appear to be manifest about 6 weeks from the beginning of the treatment.

Clinical Uses

Stimulation of mammary growth—C. M. MacBryde has been unable to find records of carefully controlled studies of growth of the breast. He found by an investigation of 3 cases that the injection of from 150,000 to 350,000 international units of oestrone or oestradiol benzoate per week produced active mammary growth where previously there had been no palpable breast tissue. Growth was even more rapid with alternate daily injections of 1 international unit of progesterone with from 20,000 to 50,000 international units of oestrone or oestradiol benzoate.

With the same purpose the author compounded an ointment of hydrous wool fat and soft paraffin containing 5,000 international units per gram of oestradiol or of oestradiol benzoate, which he applied directly to the breast region over a circular area approximately 10 cm. in diameter, radiating from the nipple. Each day 5 g. (25,000 international units) were applied by the patient to the breast region on one side, rubbed in for 5 minutes, and allowed to remain on overnight. The breast of the other side was used as a control, receiving the same amount of ointment (base without the oestrogen) and the same amount of massage. Definite mammary growth was produced by this application. Absorption into the systemic circulation was confirmed by the change of the vaginal smear from the inactive to the active oestrous state. Ointments were more effective in inducing growth than injections, and ointments containing oestrone were less effective than those containing oestradiol.

Prevention of conception.—A. S. Parkes *et al.* investigated the problem whether oral administration of oestrogens can be made effective enough to prevent or disturb implantation of the blastocyst. The preparations investigated were ethinyl oestradiol and diethylstilboestrol. Both prevented conception in rabbits. The former proved

much more potent. If given ¹/₂ after the injection, the luteal phase of the menstrual cycle was suppressed.

in the case

Yohimbine

Absence of oestrogenic activity.—H. F. Voss drew attention to the many recent publications in international medical literature attributing oestrogenic action to yohimbine. A series of experiments on castrated female mice and immature female rats showed that this assertion was untenable, yohimbine possessing no oestrogenic activity whatsoever.

MacBryde, C. M. (1939) *J. Amer. med. Ass.*, **112**, 1045.

Muhlbock, O. (1939) *Lancet*, **1**, 634.

Parkes, A. S., Dodds, E. C., and Noble, R. L. (1938) *Brit. med. J.*, **2**, 557.

Schiff, L., Elson, H., Graff, J., and Meyer, B. (1938) *Amer. J. digest. Dis.*, **5**, 292.

Varangot, J. (1939) *Pr. méd.*, **47**, 725.

Voss, H. F. (1939) *Arch. exp. Path. Pharmac.*, **192**, 570.

Wilson, L., and Kurzrok, R. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 302.

Male Sex Hormone

Methods of Administration

J. B. Hamilton and R. I. Dorfman experimented with day-old female chicks to find the solvent which produced the longest and most effective action of testosterone propionate. The action of the androgen was observed in terms of comb growth. They found that, while the group receiving 20 mg. of testosterone propionate in crystalline form exhibited a steep curve of comb growth for 71 days, with beef tallow the corresponding period with the same dose was 27 days, with mutton tallow and peanut oil 13 days, with mineral oil 9 days, and with spermaceti wax 5 days. Palmitic acid was also found to be a satisfactory vehicle. The authors suggested that implantation of pellets of the crystalline hormone might be employed for hormone therapy, instead of the more expensive and less convenient intramuscular injections.

C. R. Moore *et al.* applied testosterone and testosterone propionate to the skin of rats and guinea-pigs. It was given as a cream containing 50 mg. to the ounce. Treatment was restricted to one daily application on the shaved neck, shoulders, or belly. The area of skin selected was 2 to 6 square inches. They also gave oestradiol, in the form of a face-cream marketed for the removal of wrinkles, in daily doses of 8.2 micrograms applied to the skin. They found that both of these hormones produced typical reactions when applied to the skin. For example the testosterone re-established sexual vigour in castrated rats, and the oestradiol stimulated mammary development in normal guinea-pigs. They suggested that, in view of these activities, cosmetics containing hormones should be employed with caution.

Clinical Uses in Men

Hypogonadism and surgical castration.—A. T. Kenyon *et al.* investigated the changes in the metabolism of 4 eunuchoids produced by the intramuscular injection of 25 mg. of testosterone propionate daily. One of the eunuchoids had a large suprasellar cyst. The urinary output of nitrogen was decreased, amounting to the retention of 1.16 to 4.51 g. per day. The urinary sodium also declined, resulting in retention of 0.33 to 0.55 g. daily usually in the form of the chloride. The eunuchoids gained in weight, largely due to the water held in association with the nitrogen and sodium. The excretion of potassium and creatinine diminished in 2 eunuchoids. A slight rise of 6 to 14 points in the basal metabolic rate occurred in 3 cases. The injections produced frequent erections with increase in the size of the penis and prostate in all patients. The effects produced by the injections disappeared when the injections were discontinued.

Six cases of hypogonadism were treated by S. A. Vest and J. E. Howard with testosterone propionate; 5 showed primary testicular insufficiency due to castration, to atrophy following upon trauma, or to a defect inherent in the testes, and in one case the gonadal insufficiency was secondary to pituitary disease. In each of the 6 cases good results were obtained. The number of erections was markedly increased, normal coitus was performed, ejaculation was increased, and emissions occurred. The genitalia showed development and prostatic secretions were obtained. In most cases the secondary sexual characters became more pronounced and the mental and physical outlook of the patient was much improved. Skins became more

oily and normal sweating was induced was usually found that on cessation or lessening of treatment decrease in sexual activity occurred. The injections were given intramuscularly and varied in amount from 25 mg. per week to 25 mg. every other day. In order to maintain a satisfactory subjective status, a dose of 25 to 30 mg. per week seemed to be required.

B. Webster gives 6 case reports of adolescent hypogonadism treated with testosterone propionate. Of the 6 cases, 2 were typical of the so-called Frohlich's syndrome, and one was considered to be an instance of primary hypogonadism without history of previous disease or trauma of the testes or evidence of other endocrine disorder; 2 were bilateral cryptorchids, and one was an example of retardation of sexual development through severe constitutional disease (ulcerative colitis and a secondary anaemia). The treatment consisted of replacement of the androgenic hormones by means of intramuscular injections of testosterone propionate, given for periods ranging from 4 to 8 months. In each case increased genital growth and the promotion of secondary sexual characters occurred, with an accompanying decrease in the size of the mammary region and the abdomen. In 3 cases the total weight increased, but the patient appeared less obese than at the commencement of treatment; 25 mg. 3 times a week appeared to be an adequate dose. It is considered possible that small doses may be necessary at frequent intervals to prevent regression, but the data are not yet sufficient to make a definite statement in this respect.

Six castrates were successfully treated by W. M. Kearns with injections of testosterone propionate. The usual dosage employed was 10 mg. twice weekly, but in 2 cases only 5 mg. bi-weekly were necessary. The general health was improved, and erections and ejaculations appeared. Growth of beard was noted. In 3 to 6 weeks, regeneration of the prostate gland occurred, and within 6 to 8 months it had attained normal size. Loss reported a castrate who received 140 mg. of testosterone in a week. The resulting priapism was unrelieved by sexual intercourse. Further treatments were performed in 3 of the castrated patients and 2 cryptorchids, by inunction of testosterone ointment, each c. cm. containing 2 mg. of free testosterone. The total average dose administered by inunction was 28 mg. The ointment was applied at bedtime to a hairless area of skin, preferably the anterior abdominal wall. The same good results were obtained as with injections. Cases of hypogonadism due to cryptorchidism were treated with good results. Increase in growth of the genital organs appeared, with development of the secondary sex characteristics. The required dosage in these cases was an injection of 25 mg. twice weekly, or where inunction therapy was employed a total of 56 mg.

Prostatic enlargement—According to R. V. Day, hormone therapy, which should not be regarded as a substitute for surgical intervention in major benign prostatic obstruction, is a means of ameliorating the symptoms of hesitancy and nocturia. Ability to void a freer stream becomes possible, and Hamilton thinks this is due to muscle hypertrophy. The administration of sex hormones does not stimulate the testes to produce hormones, but has merely a replacement action which is not maintained after withdrawal of treatment, and there is abundant evidence to show that continued administration definitely inhibits internal secretion. Therefore in patients under the prostatic age intensive treatment is inadvisable. Before commencement of treatment, adequate urological examination is necessary. It is also considered advisable to inject a testis tissue extract as an activator, simultaneously with testosterone propionate.

L. P. Sharpey-Schafer and R. Shackman recorded an observation on the effect of daily injections of 100 mg. of testosterone propionate in oil for 34 days, in a man, aged 53, with an enlarged prostate. The day before the injections were begun the man's bladder had been opened and a piece of an enlarged middle lobe removed for microscopical examination. The day after the last dose of testosterone was injected, the prostate was enucleated. Microscopical examination of the tissue removed before and after the injections did not show any significant changes.

Hypertrophy of male breast—Twenty-eight males, with unilateral or bilateral hypertrophy of the breast, were treated by W. J. Hoffman with injections of testosterone propionate. Small doses of 5 mg. of testosterone acetate injected twice weekly were given in the first 6 cases, but the dosage was later increased to 25 mg. twice a week. In 14 instances complete regression occurred and in 9 cases 75 per cent regression was apparent. In 2 cases the breast became more enlarged during treatment, and in 2 others there were recurrences which, however, responded to further treatment. Regression occurred most rapidly during the first month or so of treatment,

the residual mass being slowly after the injection or become reduced. The periods of treatment extended from 2 to 36 in the case average being 14 weeks, with a total of 28 injections. In several cases the primary and secondary sexual characters were stimulated. The author considered from the results obtained that further investigations were warranted.

Organic vascular disease.—Vascular changes obtained in male castrates with testosterone propionate led E. A. Edwards *et al.* to conclude that good results might be obtained in the treatment of organic vascular disease. In 7 males, 3 of whom showed typical signs of thrombo-angitis obliterans and 4 of whom were arteriosclerotics, the administration of testosterone propionate produced marked changes. The testosterone was given by injection 2 or 3 times weekly. Arterialization of the cutaneous tissues occurred, and the volume of blood in venous areas was diminished. High blood pressures were lowered and low blood pressures raised. The ability to walk was much improved. The results obtained suggest the need of further investigations, but caution is advised in considering the application of such treatment to females.

Clinical Uses in Women

Suppression of lactation.—R. Kurzrok and C. P. O'Connell injected 21 patients in whom it was decided, early in the puerperium, to terminate lactation with testosterone propionate. The total dosage varied from 50 to 150 mg., 2 deep gluteal injections of 25 mg. each being given for one or more days. Inhibition of lactation by the usual therapeutic measures results in pain, tenderness, and engorgement of the breasts. Testosterone propionate usually relieved these symptoms in about 24 hours. A total dose of 100 mg. may be given within 48 hours, but a smaller quantity may relieve symptoms. The hormone did not otherwise affect the puerperium, and there were no unpleasant after-effects.

Menstrual disturbances.—Desmarest and Capitain have reported on their method of treatment of menorrhagia-metrorrhagia and of disturbances of the menopause by injections of male hormone, with and without folliculin. In their experience in amenorrhoea, for instance, there was a hyperfunction of the anterior pituitary and lack of folliculin, and the combined administration of testosterone and folliculin was advisable. In haemorrhagic conditions there was an excess of folliculin in the blood, and therefore testosterone in high doses alone was used with satisfactory results. In decreasing intermenstrual intervals, and increasing meno-metrorrhagia, 5 mg. of testosterone and 1 ampoule of folliculin were injected on the tenth, fifteenth, and twentieth day of the cycle. The authors reported excellent results with this therapy, which they attributed to the regulating action on the anterior pituitary of the male hormone.

Menopausal disturbances.—L. Kurzrok *et al.* treated 21 women at the menopause, both natural and artificial, by intramuscular injections of testosterone propionate in oil, 30 to 50 mg. per week were sufficient to relieve the symptoms, but 20 to 40 mg. did not prevent uterine haemorrhages. All the cases were benefited, headache, flushes, and sweating being cured or almost cured in all cases. No patient complained of any pain in, or symptoms connected with, the breasts. In one patient only was menopausal arthritis relieved by testosterone, and from their experience the authors believe that this form of arthritis responded better to the female sex hormone.

Day, R. V. (1939) *J. Urol.*, **41**, 210.

Desmarest and Capitain (1939) *Pr. méd.*, **47**, 1031.

Edwards, E. A., Hamilton, J. B., and Duntley, S. Q. (1939) *New Engl. J. Med.*, **220**, 865.

Hamilton, J. B., and Dorfman, R. I. (1939) *Endocrinology*, **24**, 711.

Hoffman, W. J. (1939) *Amer. J. Cancer*, **36**, 247.

Kearns, W. M. (1939) *J. Amer. med. Ass.*, **112**, 2255.

Kenyon, A. T., Sandiford, I., Bryan, A. H., Knowlton, K., and Koch, F. C. (1938) *Endocrinology*, **23**, 135.

Kurzrok, L., Birnberg, C. H., and Livingston, S. (1939) *Endocrinology*, **24**, 347.

Kurzrok, R., and O'Connell, C. P. (1938) *Endocrinology*, **23**, 476.

Moore, C. R., Lamar, J. K., and Beck, N. (1938) *J. Amer. med. Ass.*, **111**, 11.

Sharpey-Schafer, E. P., and Shackman, R. (1939) *Lancet*, **1**, 1254.

Vest, S. A., and Howard, J. E. (1938) *J. Urol.*, **40**, 154.

Webster, B. (1938) *J. Pediat.*, **13**, 847.

SHOCK AND COLLAPSE

See also Vol. XI, p. 126, and Cumulative Supplement, Key No. 1400.

Surgical Shock

H. Devine divided post-operative shock or collapse into 2 groups, viz. that in patients with a normal circulatory mechanism, and that in those with a crippled circulatory mechanism, e.g. due to myocardial degeneration and coronary sclerosis. He showed that in the first group shock could be caused reflexly by nervous disturbance, by some circulating toxic product, and perhaps by a sudden disturbance in the blood coagulation system.

Devine, H. (1938) *Aust. N Z. J. Surg.*, **8**, 145.

Hypothesis of Shock

In cases of shock both the blood circulation and the nervous system are important. The cause of the failure of blood circulation has not been ascertained. Gorev put forward the suggestion that the quantity of circulating blood is diminished. Experimenting on dogs and rabbits he concluded that the heart function is little affected even when the blood pressure is very low. Even after cutting the nerves of the kidney, spleen, and liver, it was found that, in dogs during shock, the kidney, spleen, and brain diminished in size, but the liver became greatly enlarged. The blood pressure in the portal vein increased from the usual 10 cm. water to 29–33 cm. The author believes that, in cases of experimental shock in dogs, the blood becomes 'blocked' in the vessels of the liver and portal veins. He concludes therefore that shock should not be treated by injection of adrenaline or other vasoconstrictor substances, but by blood transfusion or injection of Bayliss's solution (sodium chloride, 0.91, finest picked gum acacia, 6.0; and distilled water to 100, sterilized)

Gorev (1939) *Vrach. Dyelo*, **21**, 31.

SILICOSIS

See also Vol. XI, p. 133.

Morbid Anatomy

C. B. Coggin *et al.* investigated the incidence of secondary heart disease in pneumoconiosis, its frequency as a cause of congestive failure, and its clinical and radiological detection. The authors analysed 102 cases of pneumoconiosis, in nearly 20,000 necropsies, and the clinical records of 103 additional cases with adequate histories of exposure to silica and characteristic X-ray changes. At necropsy, right ventricular hypertrophy was found in approximately half of the cases of pneumoconiosis, alone it was present in 44.1 per cent of the 102 necropsies, and combined with hypertrophy of the left ventricles in 58.8 per cent. Definite congestive cardiac failure was more frequent in these cases (51 per cent) than was tuberculosis (40.2 per cent) and was usually a terminal event.

Coggin, C. B., Griggs, D. E., and Stilson, W. L. (1938) *Amer. Heart J.*, **16**, 411.

Diagnosis

From clinical observations C. B. Coggin *et al.* concluded that the clinical diagnosis of cor pulmonale (pulmonary heart disease) in pneumoconiosis is suggested by accentuation of the pulmonary second sound, prominent cyanosis, right axis deviation in the electrocardiogram, and characteristic changes in the postero-anterior radiograph, namely, prominence of the pulmonary conus, elevation of the cardiac apex, and an increase of the broad or basal diameter, in the absence of enlargement of other diameters.

Coggin, C. B., Griggs, D. E., and Stilson, W. L. (1938) *Amer. Heart J.*, **16**, 411.

Prevention

J. J. Denny *et al.* examined the manner in which metallic aluminium reduced the solubility of silicious material, and whether its action was systemic or local.

Six rabbits exposed to quartz, after the injections developed silicosis, but 7 rabbits exposed to quartz dust plus 1 in the case of metallic aluminium powder for the same period did not. It was found that metallic aluminium on being converted into hydrated alumina reduces the toxicity of quartz in tissues in 3 ways: (i) by flocculation; (ii) by absorbing silica from solution; and (iii) chiefly by coating the quartz particle with an insoluble and impermeable coating. Animal experimentation showed that the inactivation of quartz by aluminium is not a systemic reaction, but takes place only when aluminium is closely associated with quartz in body cells or fluids. Aluminium dust used for prevention of silicosis should be free from grease and have a particle size below 5 microns. The aluminium dust should be uniformly mixed in any inhaled dust, but it may be inhaled daily, independently of the silicious dust. A minimal concentration in the lung of 1 per cent of aluminium dust must be maintained. It was considered that the inhalation of aluminium dust in large quantities over long periods showed no effects on the general health of the animals, and no evidence of toxicity or tissue damage. When used in the necessary concentration to prevent silicosis it is some hundreds of times below the explosive-provoking concentration.

Denny, J. J., Robson, W. D., and Irwin, D. A. (1939) *Canad. med. Ass. J.*, **40**, 213.

SIMMONDS'S SYNDROME

See also Vol. XI, p. 145.

M. P. Foley *et al.* reported a case in a male Jew, 28 years old, of anterior pituitary tumour associated with cachexia, hypoglycaemia, and duodenal ulcer, the last being shown by radiological examination. Operation proved the presence of a chromophobe-celled adenoma which had undergone degeneration and cystic change. The tumour was first tapped, and then part of it was removed. The name Simmonds's disease was not used in connexion with the report which discussed the causation of the symptoms in detail.

Foley, M. P., Snell, A. M., and Craig, W. McK. (1939) *Amer. J. med. Sci.*, **198**, 1.

SKIN DISEASES: PHRYNODERMIA

Treatment

Vitamin A

M. V. R. Rao discusses phrynodermia, or toad-skin, which is the name given to a papulo-follicular dermatosis found in ill-nourished individuals. The exact cause of this condition is not clear, but, as it has been associated not infrequently with xerophthalmia and keratomalacia, it was thought that it might be due to deficiency of vitamin A. The author, therefore, treated 2 advanced cases with vitamin A concentrate, with a resulting marked improvement in the papular eruption. Each c cm. of the concentrate had 72,000 I. U. of vitamin A. The period of its administration ranged from 50 to 140 days. Other authors have reported that a good mixed diet with the addition of cod-liver oil has given satisfactory results. The author concludes that phrynodermia is probably nutritional in origin and that lack of vitamin A is an important factor.

Rao, M. V. R. (1938) *Indian med. Gaz.*, **73**, 461.

SKIN DISEASES: TUBERCULOSIS

See also Vol. XI, p. 193, and p. 64 of this volume.

Treatment

Rubrophen

F. Walter and Z. Oszast described treatment of tuberculous skin lesions by rubrophen, which is composed of trimethoxy-dioxy-oxytritan. It is a dark-red crystalline powder, insoluble in alcohol and in water. The drug was also used in

the treatment of tuberculosis of the skin and soft tissues. During treatment the haemoglobin content and the number of red-cells increased and the sedimentation rate improved. The results were very encouraging. Not only did the general condition of the patients improve, but the skin lesions (or the skeletal and soft-tissue lesions) all improved rapidly; moreover, in lupus there was uniform blanching without scar formation. Rubrophen treatment must be continued for at least 3 months, even if there is an apparent cure earlier. Resistant cases are subjected to another course after this period. The dose is 4 to 6 tablets daily; children under 3 are given one tablet daily; under 10 the dose is 2 tablets. In addition, an injection of the drug is administered daily, children receiving only a proportion of the ampoule according to their age. Experiments are being made on the treatment of leprosy with the same drug.

Walter, I., and Oszast, Z. (1938) *Acta derm-venereol Stockh.*, **19**, 491.

SKIN DISEASES: TUMOURS

See also Vol. XI, p. 200, and Cumulative Supplement, Key Nos. 1412-1415.

Innocent

Plantar Warts

Treatment—X-irradiation.—W. C. Popp and J. W. Olds report a series of cases of plantar warts, 63 per cent of which they claim to have permanently cured by X-ray irradiation. In 32 of the cases removal was accomplished with a total of 1,000 r of unfiltered radiation at 80 kv. The others received a smaller or greater amount of radiation. The authors advocate a technique using 100 kv., filtered by 0.5 mm. aluminium at a distance of 40 cm., the dose being 1,200 r.

Trichoepithelioma

L. Savatard gives an account of several cases of trichoepithelioma (epithelioma adenoides cysticum). In 2 instances the condition appeared in family groups. In the first the mother, 3 daughters, a son, and the third and second sons of the eldest daughter were affected. Later two grandsons and a daughter of one of them were found to present lesions. In this family all the tumours were confined to the face. In the second family group a mother, 2 daughters, 4 grand-daughters, and one grandson were affected. Six other cases reported gave no familial history of the condition. The most usual sites for these tumours in order of frequency are the face, scalp, and trunk. Many present a lobulated appearance resulting from fusion of growths which were originally separate. A close affinity is recognized between this type of benign tumour and basal-celled carcinomas but, although two distinct types of proliferation are found, sometimes in one lesion, the author feels that these are merely two variations of one condition. He considers that the original site of growth are the epidermis and hair follicles, rather than the sudorific region which is suggested by some authorities.

Naevi

Treatment—thorium-X.—H. Wendt described his results with thorium-X treatment in benign tumours of the skin. Thorium-X emanates 99 per cent of alpha-rays, being thus quite different from X-rays and radium. It is used as a lacquer and applied to the affected area by a brush or a wooden spatula, it dries quickly so that a dressing is unnecessary. The dose is 3,000 electrostatic units in 1 c.cm. The half-life of thorium-X is 3.64 days. The lacquer should be left on the skin until it scales off. The author treated with thorium-X a case of naevus verrucosus systemicus, a naevus vasculosus, and a callous scar. To obtain good results 5 to 10 treatments were necessary. In sensitive and eczematous skin, and near the mucous membranes, either an alcoholic or an aqueous solution should be used, instead of the lacquer. Before a second dose is applied the erythema should have disappeared.

Calcinosis

Treatment—sodium citrate and calcium gluconate.—Roovers reported a case of universal calcinosis and summarized the literature dealing with this very rare condition. Abnormal calcium deposits in the body are grouped into (i) circumscribed calcinosis, (ii) universal deposits; (iii) metastatic deposits; and (iv) dystrophic calcium deposits. True universal calcinosis mainly attacks younger individuals, and

is characterized by extensive abscesses after the injection in various parts of the body. Tendons, muscles, and sinews in the case involved in calcinosis and cold calcium abscesses may appear under the skin, accompanied by fever. Fistulae and ulcerations may result and the prognosis is not good. As to the treatment of this condition ketogenic diet and ammonium chloride were tried in order to cause an acid reaction in the tissues; low-calcium diet, local diathermy, ultra-violet rays, endocrine preparations, and artificial fever were all used and discarded as insufficient. Employing a new treatment the author was able to cure completely a girl aged 5. This treatment consisted in sodium citrate orally, and intravenous injections of calcium gluconate in order to increase the ability of proteins to bind calcium by dissolving it from the tissues where it is present in large quantities. This treatment proved adequate and no new calcium deposits were found after a period of control.

Miliary Lymphocytoma

R. Hallam and H. R. Vickers recorded 2 cases of miliary lymphocytoma of the skin, a rare condition, of which 21 cases only had been reported up to 1935, 2 only in British journals, and reviewed the previous reports. Miescher had suggested that a better title would be benign lymphadenoid granuloma of the skin. It was a benign condition, lasting from a few weeks to several years, and was not associated with any other morbid process. It was a distinct morbid condition and might be localized or disseminated. Several different forms had been described; of the least rare, miliary lymphocytoma of the face, a case was described in detail, in a man aged 58, the other case, the lesion was much rarer, miliary lymphocytoma of the skin, was illustrated by a description of a woman, aged 26.

The condition must be diagnosed from (i) miliary disseminated lupus of the face, (ii) Boeck's miliary sarcoid, (iii) epithelioma adenoides cysticum, (iv) adenoma sebaceum, (v) syngo-cystadenoma, (vi) hydrocystoma, and (vii) leukaemia of the skin; it was definitely stated that no true case had been associated with lymphoid leukaemia.

F. F. Hellier described a further case of lymphocytoma of the face in a woman, aged 65, after a severe blow on the face. There were multiple small translucent lumps which were composed of lymphoid tissue; before the examination and at histological examination, the condition was thought to be cystic benign epithelioma, or Brooke's disease; the blood did not show any evidence of leukaemia. Previously the condition had been described as pseudo-leukaemia by J. Jadassohn. The name lymphocytoma was given to it by M. Kaufmann-Wolf.

Hallam, R., and Vickers, H. R. (1939) *Brit. J. Derm.*, **51**, 251.

Hellier, F. F. (1939) *Brit. J. Derm.*, **51**, 260.

Jadassohn, J. (1906) *Arch. Derm. Syph., Wien*, **82**, 297.

Kaufmann-Wolf, M. (1921) *Arch. Derm. Syph., Wien*, **130**, 425.

Miescher, G. (1937) *Bull. Soc. franç. Derm. Syph.*, **44**, 1254.

Popp, W. C., and Olds, J. W. (1938) *Radiology*, **31**, 218.

Roovers, J. J. C. P. A. (1939) *Acta med. scand.*, **100**, 57.

Savatard, L. (1938) *Brit. J. Derm.*, **50**, 333.

Wendt, H. (1939) *Derm. Wschr.*, **108**, 10.

Malignant

Squamous-Celled Carcinoma

Treatment. radium therapy.—I. G. Williams defined epidermal tumours of the skin as those which arise from the epidermis, and were also called epithelioma and acanthoma. A series of 214 cases was studied. The face and cheek were found to be the commonest sites with the ear relatively common. The largest group was composed of squamous-celled carcinomas, preceded by keratotic changes in the skin, and occurring mostly in those who are exposed to changing atmospheric conditions. The primary growths are invariably radio-sensitive, but the glandular metastases show a high degree of resistance. Other types of epithelioma are tar and soot carcinomas; lupus carcinoma; X-ray carcinoma; squamous-celled carcinomas in scar tissue; squamous-celled carcinomas superimposed on chronic ulceration; epidermal carcinoma associated with other new growths. In the case of tar and soot carcinomas, if radiotherapy was used, primary healing was obtained. Surface application of radium is advised in lupus carcinoma, using an accurately fitting applicator made of light porous material, such as nidrose. A full carcinoma-lethal dose of 6,000 to 8,000 r is aimed at in all cases, spread over

18 to 21 days, and applied for 16 out of 20 cases. A similar treatment has been found effective in X-ray carcinoma.

Melanotic Carcinoma

Treatment: Radio-sensitivity.—F. Ellis analysed 38 cases of malignant melanoma treated at the Sheffield Radium Centre in the years 1931 to 1937. After a review of published opinions, chiefly to the effect that these tumours were radio-resistant, the 38 cases were divided into 6 groups: (i) 12 in which success followed radiotherapy, (ii) 2 in which such success was doubtful, (iii) 7 failures, (iv) 6 in which the evidence was indefinite, (v) 7 treated after removal of an eye for a melanoma; these were really the same as in group iv, but were separately described because there was not any evidence that malignancy existed at the time of radium treatment, and also to show that no cases were withheld, and (vi) 4 cases not treated.

The possible causes of failure were critically considered and divided into (i) those due to interference from outside the patient, such as trauma including operation, infection, and excessive irradiation by damage to, and impairment of, the surrounding normal tissue cells. (ii) Those inherent in the biological material, all the patients proved to be radio-sensitive were over 42 years of age, the average age being 58½ years, whereas in the insensitive and doubtful cases the average age was 47 years. The areas involved in the radio-sensitive group were mainly more vascular than those in the insensitive group. How far the histological structure was important was difficult to decide, there was, however, a relatively higher proportion of endotheliomatous growths in radio-sensitive cases and of the sarcomatous growths in the insensitive cases, but this might not be of significance. The general resistance factor, the patient's own 'treatment' for any tumour, was probably the most important, such a factor did exist, but could not be accurately defined or estimated.

Ellis, F. (1939) *Brit. J. Radiol.*, **12**, 327.

Williams, J. G. (1938) *Brit. J. Radiol.*, **11**, 641.

Innocent Infective Conditions

Boeck's Sarcoidosis

H. B. Stallard and C. B. V. Tait reported a case of Boeck's sarcoidosis occurring in a woman of 44. The patient had a hard discrete lump in her right breast and enlarged axillary and cervical glands. Later she developed a bilateral axillary and cervical lymphadenopathy. Biopsy of the lump in the breast and a cervical gland showed sarcoid tissue. She also had complicated cataract, keratitis, and bilateral iridocyclitis. The condition progressed to secondary glaucoma and ultimately ended in phthisis bulbi. At one time she had swelling of the parotid glands and fluid in both knee-joints. Later in the disease lesions appeared in the skin and the picture became complicated by the presence of myxoedema. Microscopically the lesions are characterized by nodules consisting of a central mass of endothelial cells surrounded by lymphocytes, and very rarely a giant cell of Langhans type. There is no caseation and no tubercle bacilli have been found. A mild anaemia may be present in the condition and moderate mononucleosis, eosinophilia, and an increase in plasma globulin occur in some cases. The cause of the condition is unknown but it may belong to the group of diseases of the reticulo-endothelial system which includes lymphadenoma and uveo-parotitis. However, unlike lymphadenoma, the condition is not malignant but is subject to remissions and may terminate, except for ocular sequelae, in complete recovery.

R. Bodley Scott reported 8 new cases of Boeck's sarcoidosis which was defined as a generalized disease in which enlargement of the lymphatic glands, spleen, infiltration of the skin, lungs, and bones of the fingers, enlargement of the parotid and lacrimal glands, and iridocyclitis were manifestations. The uveo-parotid syndrome of Heerfordt was a variant of sarcoidosis. There was not any convincing evidence that the disease was a manifestation of tuberculosis; it was a disease of the lympho-reticular (reticulo-endothelial) tissue, and in the same category as leucosis and Hodgkin's disease. It was sufficiently common to interest general practitioners; out of 300 cases in which lymphatic glands were submitted for histological diagnosis at St. Bartholomew's Hospital one case of sarcoidosis occurred for every 11 cases diagnosed as Hodgkin's disease. The patient might, from its various manifestations, consult dermatologists or ophthalmologists rather than general medical men. The lymphatic glands were enlarged at some period of this extremely chronic and benign disease; the glandular enlargement

was moderate but generalized after the injury were not painful or tender, and might diminish in size while the patient was under observation. The splenic enlargement, present in 5 of the 8 new cases, might have been the real lesion in cases formerly recorded as chronic splenomegaly with military tuberculosis of the lungs. Though the skin was not involved in more than half the cases, the lesions were often very bizarre and appeared in several forms, (i) the military lupoid (Boeck), (ii) lupus pernio (Besnier), (iii) angio-lupoid, and (iv) erythrodermie sarcoïdique. The disease ran a very prolonged course. Iridocyclitis occurred in about 10 per cent of the cases. It was difficult to evaluate the result of treatment in a disease showing spontaneous evolution. Radiotherapy and gold injections were sometimes followed by improvement, and antileprol had been favoured.

Heerfordt, C. (1909) *Arch. Syph., Berlin*, **70**, 254.

Scott, R. B. (1938) *Brit. med. J.*, **2**, 777.

Stallard, H. B., and Tait, C. B. V. (1939) *Lancet*, **1**, 440.

SPEECH DEFECTS

See also Vol. XI, p. 294.

Stuttering

Ætiology

S. Cobb and E. M. Cole reviewed the probable methods of production of stuttering. Seventy-five per cent of men are right-handed, the rest being left-handed or ambidextrous. Dominance of the left cerebral hemisphere is found in right-handed people, though this dominance is only relative. In these people the left hemisphere is also dominant in speech. Five levels at which speech is integrated have been recognized. The neuro-muscular level is concerned with the actions of such structures as the larynx and palate in speech; paralysis of these results in various degrees of aphonia. The cortico-bulbar neurones constitute the next level and lesions here produce dysarthria. The cerebellum is a co-ordinating mechanism in speech and lesions here cause asynergia resulting in such symptoms as 'scanning' and monotonous speech. At the cerebral level agnosia and aphasia result from lesions. The level at which the lesion occurs in stammering is unknown. Evidence shows that it is concerned with emotional repression and with dominance of one cerebral hemisphere, or lack of clearly defined dominance. Thus a left-handed child forced to use its right hand often stammers.

Three main suggestions have been made of the cause of stammering. The first, and oldest, is that stammering results from an upset in the peripheral mechanism of speech. From this school of thought developed the psychological school, which considered stuttering a neurotic manifestation in response to a conflict. The third point of view is that the defect is neurological in origin. Speech is looked upon as part of language including, not only hearing and understanding speech, but also reading and writing. No lesions have been found in the brains of stutterers, but support is given to this theory by the facts that stuttering is often inherited and therefore some inheritable physical defect may account for it, and difficulty in learning to read, talk, or write may also occur in the patient or in other members of his family. The patients' inherited cerebral dominance may not be clearly defined and this results in the above symptoms. A clearly defined right dominance resulting in left-handedness does not, as a rule, produce stammering.

In deaf patients—It has commonly been supposed that deaf people do not stutter. Various reasons have been given for this, including the fact that speech in the deaf is scanning and that stuttering does not occur in scanning speech, that the deaf child is so handicapped that he does not usually think faster than he is able to speak, and that deaf children are taught to speak properly in language schools, unlike the child with normal hearing. However, stuttering does occur in deaf subjects. O. Backus quotes Voelker as reporting a case of stuttering in a congenitally deaf boy and, by means of a questionnaire to schools for the deaf in America, he discovered 55 cases of deaf stutterers, the large majority of whom were males, as is usual among stutterers. The cause of the stuttering is at present unknown but, since high fever may initiate stuttering and may also accompany diseases resulting in deafness, it was suggested that it might be an ætiological factor.

Backus, O. (1938) *Ann. Otol., etc., St. Louis*, **47**, 632.

Cobb, S., and Cole, E. M. (1939) *Physiol. Rev.*, **19**, 49.

Treatment of Speech Defects General**Psychological Treatment**

J. S. Greene considered the psychiatric treatment of stuttering, psychophonaesthesia, hysterical aphonia, and the falsetto voice. All the patients treated were neurotics of the sympathetic type. Characteristics of these patients were a constant state of nervous tension, lability of the pulse and blood pressure, tachycardia under emotional stress, cold clammy hands and feet, and a marked tendency to fatigue. Stuttering is due to a neurosis in which the balance of the mental, emotional, and physical states is disturbed, and there is a striving for dominance between the intellectual and emotional powers. Thus, under stress, the patient shows stutter behaviour. The defect is one of the entire personality and should be treated as such. Psychophonaesthesia, or weakness of the voice, is the manifestation of anxiety and a fear of inferiority in a neurotic patient. This fear leads him to overuse his larynx to compensate for his inferiority, this makes the larynx too powerful and a wrongly developed and a weak voice results. Hysterical aphonia is a conversion hysteria generally used to defend or remove the patient from unpleasant circumstances. Falsetto voice, of psychological origin, is due to excessive sensitivity at puberty. The boy is shocked and embarrassed by his general body changes and subconsciously tries to remain as much like a child as possible by retaining the childlike voice. Through constant use of his high voice, he alters the structure of his larynx and the voice remains permanent. Greene gives examples of cases of hysterical aphonia and falsetto voice. The prognosis in stuttering, hysterical aphonia, and falsetto voice is very favourable, but in psychophonaesthesia it is not good because the disorder is usually deeply ingrained psychically and deeply intertwined with environmental conditions. The treatment of all these conditions is psychological, aided by some measure of local treatment.

Greene, J. S. (1938) *Ann. Otol., etc., St. Louis*, **47**, 615

SPINAL CORD DISEASES

See also Vol. XI, p. 302, and p. 120 of this volume

Compression**Hernia of Nucleus Pulposus**

F. Jaeger reported 4 cases of herniae of the nucleus pulposus of the intervertebral discs, which caused symptoms and signs of acute sciatica that were resistant to all therapy for a number of years. In one case the patient could obtain relief only by lying on his abdomen and even in this position he felt pain and a certain amount of weakness in his left lower extremity. The fact that the condition remained unimproved after all known methods of treatment of sciatica was the chief diagnostic indication of an intervertebral disc lesion. It was not possible to make an exact diagnosis before the operation though contrast filling of the theca showed a block to the lipiodol (iodized oil) between the 4th and 5th lumbar vertebrae; this sign, however, is not absolutely indicative of a posterior hernia of the nucleus pulposus, because at one operation it was found to have been caused by a small fibrinous haematoma pressing on the cord. In the author's view the origin is not entirely traumatic; it seems to be superimposed on a pre-existing diseased disc.

Jaeger, F. (1939) *Munch. med. Wschr.*, **86**, 991.

Subacute Combined Degeneration

T. Rothfeld described a case of subacute combined degeneration in a man aged 59. He had duodenal ulcers at 23; later pyloric stenosis developed. Blood examination showed no abnormality but free hydrochloric acid was absent from the stomach. The patient was cured by betaxin (vitamin B₁₂), and extract of liver and of stomach. Some deficiency, perhaps of amino-acids, was the cause of the nervous signs in this case. An ulcer has been observed in many cases but nervous symptoms have been a rare complication. Subacute combined degeneration has sometimes been observed in brothers and sisters, none of whom showed abnormality in blood or intestinal tract. Subacute combined degeneration may also be combined with atrophy of the optic nerve. Subacute combined degeneration is a deficiency disease but the deficient substance is different from the anti-anaemic substance. It may

develop in the course of pylemia after the injection demonstrated by this case. Two forms of subacute combined degeneration in the case are distinguished, a genuine form resulting from heredo-generation and a syphilitic form occurring in pernicious anaemia and other diseases.

Rothfeld, T. (1938) *Conf. neurol.*, **1**, 243.

Familial Neuromyelitis Optica

D. McAlpine described the case of a girl who became affected by neuromyelitis optica at the age of 24 years; she died eighteen months later. Her identical twin sister developed the same condition at the age of 25 years, and died 26 months after the onset. Demyelination was observed in the spinal cord as well as in the optic nerves of both cases. The grey matter as well as the white matter was affected. Perivascular or meningeal infiltration was not seen in the first case, and was very slight in the second.

Neuromyelitis optica differs from the other demyelinating diseases, such as Schilder's disease, acute disseminated encephalomyelitis, and disseminated sclerosis. Apart from the rare occurrence of discrete demyelination in the brain stem, and an occasional vessel showing perivascular infiltration there and in the basal ganglia, the rest of the nervous system shows no notable morbid change. In neuromyelitis optica the morbid process is as a rule more intense than in disseminated sclerosis. In acute disseminated encephalomyelitis the lesions are more wide-spread. If the condition is due to a virus or its toxin, both cases described in this paper may have harboured the virus independently, or the second patient may have been infected by her sister.

McAlpine, D. (1938) *Bram*, **61**, 430.

Chronic Adhesive Spinal Arachnoiditis

R. P. Mackay described 5 cases of chronic adhesive spinal arachnoiditis. Three of the cases followed acute meningitis, probably meningococcal, and there was one death in this group. Of the other 2 cases arising spontaneously, one died. Necropsy showed thickening and adhesions and sometimes cyst formation in the leptomeninges. Thickening and occlusion of the blood vessels occurred with areas of degeneration and softening in the substance of the spinal cord. The arachnoiditis caused pain, paraesthesias, muscular twitchings, and sensory disturbances at the level of the cord affected. The tendon reflexes were inconsistent, some being diminished and some exaggerated in the same patient. If only a localized arachnoid cyst is present surgical treatment is successful, but in the later stages of the disease when there are many adhesions it may be harmful.

Mackay, R. P. (1939) *J. Amer. med. Ass.*, **112**, 802.

SPINE, DISEASES AND DEFORMITIES

See also Vol. XI, p. 361.

Tuberculosis

Treatment

Surgical. W. E. Swift reviewed the results of treatment of 309 children under 10 years of age, with active tuberculosis of the spine, on whom Hibbs' spinal fusion operation had been performed, 74 per cent of the patients showed good results. Most of the children completed their stay in hospital and no longer needed a spinal support in 10 months. In successful cases the child led an active normal life after operation, without any symptoms or physical signs referable to the spine apart from deformity and limitation of movement in some cases. X-rays showed complete subsidence of the local condition. Swift believed that the area of tuberculosis in the spine could be considered cured after a successful fusion operation and that there would be no recurrence in that area.

Paraplegia

Surgical treatment.—G. Nystrom reviewed the causes of compression of the spinal cord in tuberculosis of the spine, and stated that a cautious laminectomy can sometimes restore to health patients who otherwise would remain permanently

paraplegic. A case is mentioned in whom 18 months' conservative treatment did not produce any change in the paraplegia. Later, following a tuberculous process of the first and second thoracic vertebrae, a laminectomy was resorted to, and the tuberculous foci were removed and curetted away. Movements returned after 2 months. The author warned against being too dogmatic in denying the use of surgical methods in the treatment of early paraplegia in tuberculous spondylitis.

Nystrom, G. (1939) *Acta chir. scand.* **82**, 159.

Swift, W. E. (1938) *J. Pediat.*, **13**, 248.

Prolapse of Intervertebral Discs

W. G. Douscher and T. G. Love examined the annular lamella as well as the nucleus pulposus in parts of posterior prolapses of intervertebral discs which were removed at operation. Marked degeneration was sometimes observed in the cartilage cells of prolapsed tissue, especially in senile individuals. Slight degeneration and fibrosis were then observed. The fibrous tissue may be connected with notochordal rests. A decision could not be made as to whether the notochordal tissue was replaced by fibrous tissue or whether the notochordal cells had changed into cells looking like fibrous-tissue cells. Fibrous tissue was, however, sometimes observed without any connexion with the rest of the notochordal tissue. Oedematous swelling may be observed in the prolapsed tissue, as well as in the nucleus pulposus and annular lamella. It probably results not only from the great capacity of the nucleus pulposus for swelling, but also from disturbed circulation in the prolapse. Oedematous swelling and decrease, arising in the prolapsed intervertebral discs, often caused increased symptoms or repeated attacks of pain.

Douscher, W. G., and Love, T. G. (1939) *Schweiz. Arch. Neurol. Psychiat.*, **43**, 8.

Scoliosis

J. Dewey Bisgard divided preventable deformities of the thoracic spine into two groups, pleurogenic and thoracoplastogenic. Pleurogenic scoliosis differs from all other types in that there is little, if any, rotation of the vertebral bodies. The thoracoplastogenic form is of the rotatory type. Although most patients with pleural diseases, many with pulmonary disease, and all who undergo extensive costal resections develop some curvature, few progress to a stage of deformity. Adults are rarely affected, the majority of cases occurring in children and adolescents. Either type is curable in its incipient stage, but extensive and rigid deformities of the spine and costal framework are incurable. Pleurogenic deformities may be prevented by (i) prevention of the formation of pleural scars by early care of the empyema or pleurisy, and (ii) constant attention to maintenance of straight alignment or, preferably, over-correction of the spine. Correction might be accomplished by means of posture, aided by wedging. The use of Bradford frames for securing postural correction is recommended. Should the curvature persist after the patient becomes ambulatory a special type of plaster jacket is advocated. In the case of children a plaster bed is moulded to the body and used in conjunction with postural wedging. The resection of ribs on the side of the concavity sometimes corrects curvature. Thoracoplasty scoliosis is prevented and corrected by postural wedging instituted a few days after the operation and maintained for at least 6 weeks. The early use of corrective measures may be facilitated by anaesthetizing the area of the wound by crushing the intercostal nerves supplying it.

Bisgard, J. D. (1938) *Tubercle, Lond.*, **20**, 13.

Spondylolisthesis

Spondylolisthesis (slipping vertebra) was defined by Ziegler as 'a deformity in which, by the action of the weight of the trunk, the body of the fifth lumbar vertebra and the portion of the spinal column above it slips forward over the base of the sacrum'. K. Speed reported a case successfully treated by anterior fusion of the bone, the bone graft being taken from the tibia, and reviewed the subject.

The condition might be caused by trauma; local infection and muscular fatigue, temporary overstrain, and possibly defective ligamentous support might play a part. Lumbosacral pain, stiffness in the back, shortening of the spine, a crease across the back, and depression over the fourth or fifth lumbar vertebrae resulted. The abdomen was proportionately protuberant and the gait might become waddling.

The condition was readily after the injury. The treatment might be palliative or curative. Traction the case and feet in recumbency had resulted in reduction of the deformity. Posterior spinal fusion both by Hibbs' and Albee's method had been employed. Some success was obtained in these cases, but this posterior fixation did not mean that the anterior part of the fifth lumbar vertebra might not in time plunge forward and rotate down in front of the sacrum. Successful attempts had therefore been made to fuse anteriorly the body of the fifth lumbar vertebra with the sacrum.

Speed, K (1938) *Arch. Surg., Chicago*, **37**, 175

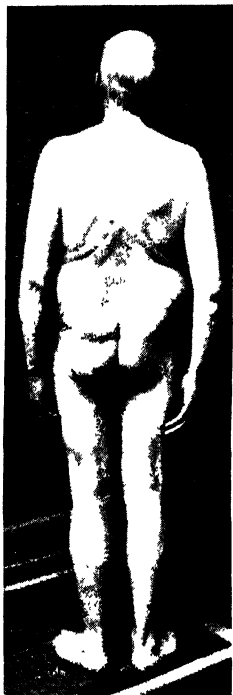


FIG. 24 — Meulengracht's patient, showing the deformities resulting from skeletal collapse (From *The Lancet*, 1938)

Osteomalacia

Actiology

E. Meulengracht reported a case of osteomalacia of the spine in an engineer aged 71 following the long-continued abuse of laxatives. X-rays showed a row of coalescing vertebrae with a number of hour-glass-shaped vertebral bodies and without any normal lumbar vertebrae. The usual persistent pains in the back were present with numbness in the lower extremities. The spinal collapse was progressive, the patient becoming 10 to 12 cm. shorter. Leather and fabric corsets with iron supports had been used to impart firmness, and analgesics to relieve the pain. The patient's diet had been rather rich, though red meat and meat soups had been restricted for fear of 'gout'. He was prosperous and there was no economic motive for an unbalanced diet. The explanation given was that the patient had regulated his bowels daily for 35 years with one teaspoonful of 'Carlsbad' salts. This mixture of sodium sulphate and sodium bicarbonate had transformed some of the calcium in the food into calcium sulphate, the passage in the motions of this calcium in the form of 'calcium soap' and its non-absorption for skeletal maintenance resulted in the calcium deficiency and consequent osteomalacia. The patient's condition thus resembled coeliac disease and sprue in which a certain amount of calcium is precipitated in the form of calcium soap and therefore not absorbed.

Meulengracht, E. (1938) *Lancet*, **2**, 774.

SPLEEN DISEASES

See also Vol XI, p. 401.

Accessory Spleens

R. F. Robertson reviewed the characters of accessory spleens. Although rarely reported by the surgeon, they are said to occur in 10 or 11 per cent of necropsies. They vary in number, and Albrecht has described a case in which 400 were present in various situations in the peritoneal cavity. The commonest positions in which they are found are at the hilum of the spleen, in the gastro-splenic ligament, in the splenocolic ligament, in the pancreatic-splenic ligament, in the great omentum, along the blood vessels of the spleen, and in the gastro-hepatic omentum. They have also been found on the transverse colon, and embedded in the pancreas and the liver. In Albrecht's case many of them were in the pouch of Douglas, but all the spleens found were enveloped in a covering of peritoneum, and showed the macroscopical and microscopical appearance of splenic tissue.

The accessory spleens are held by some to develop from splenic particles displaced by trauma and implanted on or into other structures. The trauma may be intra-

uterine. Other authorities hold that they are congenital anomalies. They are often associated with other developmental anomalies. If the main splenic tissue becomes deficient, these accessory spleens undergo hyperplasia. They are more commonly found in children than in adults, probably because they undergo atrophy later in life.

These spleens may be of clinical importance, and Robertson reported 5 cases in which they gave rise to symptoms. Two of the patients complained of abdominal pain which was attributed to interference with the blood supply of the part to which the accessory spleen was attached. Two other cases were of purpura haemorrhagica; one was followed by apparent cure almost 3 years after splenectomy, and the other showed signs and symptoms of the condition nearly 2 years after operation. The latter was found to have an accessory spleen near the hilum of the spleen, which was not removed. The fifth case was one of partial obstruction due to pressure from an accessory spleen on the splenic flexure. Peritonitis resulted, and bands were formed which further obstructed the lumen.

Robertson, R. F. (1938) *Canad. med. Ass. J.*, **39**, 222.

Reticulo-Endotheliosis of the Spleen

The reticulo-endothelial system may be implicated in many pathological conditions. Among these are disturbances of the function of storage as in Gaucher's disease, infectious proliferative granuloma as in Hodgkin's disease, hyperplasia as in monocytic leukaemia, and dysplasia as in the so-called reticuloma and endothelioma. In addition, proliferation of the reticulo-endothelial system may occur in specific diseases such as syphilis.

M. S. Sacks reported a case of the rare condition, reticulo-endotheliosis, or systemic proliferation of the reticulo-endothelial system. The condition is characterized by proliferation in all the elements of the system and is most marked in the spleen, lymphatic glands, liver, and bone marrow. One chain of lymph glands, such as the cervical, is often involved more than the others. The glands are usually discrete and do not invade neighbouring structures. Among other rarer and less important manifestations are petechial or purpuric haemorrhages, early cirrhosis of the liver, and localized masses either in the viscera or over the bones.

The disease may occur at any age but the majority of cases are encountered in infants and young children. The sex incidence is about equal. The onset is insidious and is often first noticed after some infection. Weakness and fever are the usual complaints. Blood examination shows a hypochromic anaemia and the leucocyte count is normal or reduced. A monocytosis has been observed. X-ray examination shows rarefaction and sometimes cysts of affected bones. These investigations combined with biopsy form the best methods of diagnosis. The aetiology of the condition, and whether it is inflammatory or neoplastic, is unknown. Sacks reported a typical case occurring in a man of 51 years who died of heart failure 18 hours after admission to hospital.

Sacks, M. S. (1938) *Arch. Path.*, **26**, 676.

Werlhof's Disease (Purpura haemorrhagica)

Aetiology

Werlhof's disease consists in thrombopenia secondary to primitive splenomegaly. M. Torrioli and V. Puddu found that highly concentrated extracts of spleen from these patients injured the megakaryocytes in cultures *in vitro* of the bone marrow of guinea-pigs. On the other hand small doses of the splenic extract stimulated the megakaryocytes. They later found that the normal spleen contained the same principle, though it was less active, and that in other tissues the amount of it present was proportional to their content of reticulo-endothelial tissue. It was also shown that this principle occurred in blood taken from the splenic vein of patients suffering from Werlhof's disease. Normal spleen was shown to have a principle which would reduce the number of platelets circulating in rabbits when introduced intravenously. It was assumed that this principle was in excess in the spleen in Werlhof's disease and that splenectomy would therefore result in a return to normal.

Torrioli, M., and Puddu, V. (1938) *J. Amer. med. Ass.*, **111**, 1455.

after the injection
the case of STERILITY

See also Vol. XI, p. 447; Cumulative Supplement, Key Nos. 1455-1457; and pp. 30 and 157 of this volume.

Sterility in the Female

Investigation of Patients

Excretion of pregnandiol.—A. A. Hain and F. M. Robertson correlated histological examination of endometrial scrapings with the estimation of the excretion of pregnandiol in the urine of 5 sterile women. It had been found previously that a subnormal excretion of pregnandiol and a short luteal phase were associated with sterility. Pregnanndiol excretion is directly related to corpus luteum activity. None is found in the first half of the menstrual cycle. The amount in the second half of the cycle varies from 3 to 60 mg. It is invariably associated with a secretory and not a proliferative endometrium. In 2 of the patients there was evidence of a subnormal excretion of pregnandiol.

Treatment

Tubal resection and implantation.—A. H. Curtis discusses the cause and surgical relief of sterility in women and considers gonorrhoea of prime importance. Other aetiological factors are infections resulting from abortions and inflammatory processes resulting from post-abortive curettage. Provided that the patient is in good general health and the husband fertile, surgical intervention is advised for the relief of sterility. The author emphasizes the value of correcting a diseased cervix and describes a method of tubal resection and implantation whereby access to the uterine cavity is gained by lateral perforation of the uterus immediately below the level of the tube, which has been bisected and its uterine end elevated like an elephant's trunk. This procedure obviates the necessity of excising the diseased indurated interstitial part of the uterine cornu.

Curettage.—L. Kraul stated that curettage in sterility was mainly an 'irritative' measure and that in some women the passage of a sound into the uterus was alone sufficient to cure the sterility. Curettage influenced the ovarian cycle and in most cases menstruation occurred exactly 4 weeks after curettage. There was a connexion between the hormonally controlled menstruation and maturation of the follicle, and mechanical irritation of the uterus. The author curetted the uterus not only for the treatment of sterility but also for diagnostic purposes. The curettage was performed during the pre-menstrual period, as near as possible to, but before, the menstruation. A mucous membrane in the stage of hypertrophy and hyperplasia, representing a transition to that of metropathia haemorrhagica, was very often connected with cystic degeneration of the ovaries, indicating treatment with 10 mg. of oestradiol benzoate. Other findings were a decidual mucosa due to extra-uterine pregnancy, endometritic mucous membrane, miliary endometrial tuberculosis, and adeno-carcinoma.

Utilization of fertile period of cycle.—In order to determine the exact time of ovulation and therefore to be able to plan conception in fertile women, T. T. Zuck investigated the temperatures of 67 women. The temperature was taken *per rectum* daily, just before rising. Just before menstruation there was a slight fall in temperature, in most women to 98° F., which was maintained during the flow. At the end of the period there was perhaps a temporary fall of the temperature which then rose to somewhat above 98° F., and dropped abruptly at the mid-period to its lowest level, 97° F. or even lower. It then rose to just above 98° F. and remained practically stationary until the onset of the next menstrual period. This temperature variation was characteristic of 80 per cent of the women studied. Mid-period indications, including discomfort or pain in the lower abdomen, vaginal discharge or haemorrhage, headache and sleeplessness, and subjective feelings caused by rupture of the follicle, were stated to be experienced by 50 per cent of the women and were considered to coincide with ovulation. No pregnancy occurred before the eleventh or after the eighteenth day of the cycle. Pregnancies resulting from single coitus indicating the time of ovulation in individual women were recorded. It was concluded that the viability of the ovum is not more than 36 hours and of the sperm less than 24 hours, and that morning sickness begins at the computed time of the next ovulation period after conception and might therefore be related to a change in the ovulation cycle.

Artificial insemination.—F. I. Seymour reported a case of sterility occurring in the

presence of motile spermatozoa which passed through the cervical canal after intercourse. Both husband and wife were negative for every clinical and bacteriological test. Treatment with a diet rich in vitamins, exposure to sunlight, and change of environment did not produce pregnancy. Subsequently sterile women volunteered to be artificially inseminated with the husband's semen every month but they did not become pregnant; the wife, however, became pregnant after insemination from another male.

Curtis, A. H. (1938) *Arch. Path.*, **26**, 354.

Hain, A. A., and Robertson, L. M. (1939) *Brit. med. J.*, **1**, 1226.

Kraul, L. (1939) *Wien. med. Wschr.*, **89**, 35.

Seymour, F. I. (1939) *J. Amer. med. Ass.*, **112**, 1817.

Zuck, T. T. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 998.

STERILIZATION

See also Vol. XI, p. 467; Cumulative Supplement, Key Nos. 1458–1460, and p. 158 of this volume.

Sterilization of the Female

Operative Methods

A method of reopening ligated uterine (Fallopian) tubes without recourse to laparotomy was recommended by I. C. Rubin. Uterotubal insufflation with carbon dioxide has been successful in cases of involuntary sterility due to strictures and peritubal adhesions, and can be employed to re-establish tubal patency after surgical sterilization. The more recent the ligation, the less the pressure required to reopen the tubes. Patency was re-established in 5 cases, following ligation, by pressures less than 160 mm. Hg. Unless the interstitial portion of the tube has been resected, the artificially induced obstruction should yield to insufflation at a pressure of 200 mm. Hg or less, and in experienced hands, the pressure level may be increased to 250 mm. Hg. If failure occurs on the first attempt, insufflation can be repeated at suitable intervals. The flow of carbon dioxide should be at the rate of 1 c.cm. per second or slower, the rise of pressure and reaction to pain being watched. About 100 c.cm. of the gas is adequate and insufflation occupies from 2 to 3 minutes on the first occasion. Fluid mediums may be used instead of carbon dioxide but their pressure control is not as accurate and their injection cannot be repeated with so much safety. Skiodan (abrodil), hippuran, or any rapidly absorbable crystalloid compound of iodine was recommended, and can be injected with the aid of the kymographic insufflation apparatus.

Rubin, I. C. (1938) *J. Amer. med. Ass.*, **111**, 1999.

STOMACH, TUMOURS AND SOME OTHER CONDITIONS

See also Vol. XI, p. 476.

Malignant Tumours

Treatment

Surgical.—H. B. Neal and J. M. Waugh of the Mayo Clinic reported a case of total gastrectomy for primary carcinoma and quoted Walters' indications for this operation, namely (i) the growth should be confined entirely to the stomach and without evidence of metastases; (ii) there should be sufficient gastric and lower oesophageal mobility to ensure a satisfactory oesophago-jejunal anastomosis; and (iii) the patient should be in a sufficiently good general condition to withstand the severe shock involved. For an operation to be classified as a complete resection the cardiac and pyloric sphincters must be removed with the intervening part of the stomach. If a small portion of stomach not exceeding 3 cm. remained, the operation was classed as subtotal gastrectomy, and if more than 3 cm. of stomach was left, as a partial gastrectomy. It was remarkable how efficiently the jejunum took the place of the removed carcinomatous stomach. From 1917 to December 1st, 1938, 30 total gastrectomies were performed at the Mayo Clinic. The sequel of grave anaemia, which did not occur in all cases, was reported by Moynihan and W. J. Mayo long before the discovery that pernicious anaemia was due to absence of an intrinsic

factor secreted by the pylorus after the injury of the stomach and duodenum. The mortality of complete resection reported in the case of 29 was 54 per cent. The longest post-operative survival had been 4 years and 8 months, but the usual duration was 2 years and in most of the patients the carcinoma recurred. There are several variations in the operative technique; for instance posterior colic oesophago-jejunostomy with a jejunostomy tube for temporary feeding, and an anterior colic oesophago-jejunostomy with jejuno-jejunostomy have been used

Leiomyoma

G. Ball recorded a case of leiomyoma of the stomach in a man, aged 65, who had had severe haematemesis and anaemia. Radiologically there was a filling defect high up on the lesser curvature. At an exploratory laparotomy a large sessile tumour 4.5 by 4.0 by 3.0 cm. was found, covered by mucosa which was not grossly ulcerated but showed a small hole opening into a cavity in the tumour, containing blood. Microscopically the tumour showed many areas of hyaline degeneration which probably accounted for the central cavity. Fifteen months later the patient was in good health.

Ball, G. (1939) *Brit. J. Surg.*, **26**, 942

Neel, H. B., and Waugh, J. M. (1939) *Proc. Mayo Clin.*, **14**, 129.

Acute Dilatation

According to Hamilton Bailey acute dilatation of the stomach was a fairly frequent post-operative complication and might follow any operation, formerly it was most

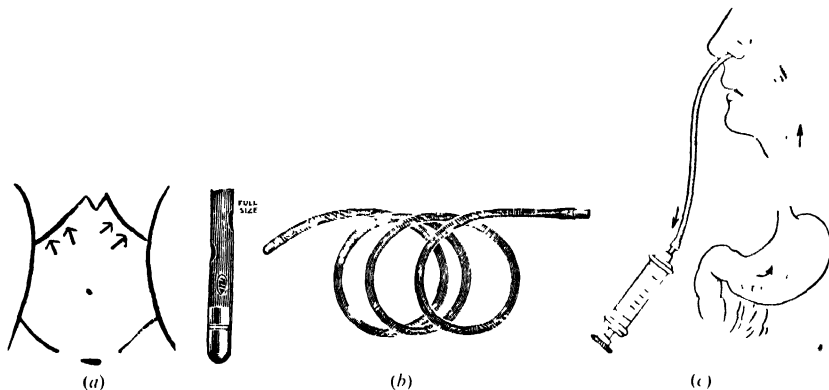


FIG. 25 (a) Obliteration of the normal slight concavity beneath the costal margin is a somewhat characteristic sign in acute dilatation of the stomach. (b) Bailey's tube for continuous aspiration of the stomach via the nasal route. There is a coiled spring within the distal end of the tube to stiffen it. This aids considerably in its passage from the nostril to the stomach. (c) Drainage of the stomach via the nose. (From *British Medical Journal*, 1939)

often seen after those on the biliary tract, but now perhaps prostatectomy headed the list. Early diagnosis was important and could be made before the occurrence of vomiting which was a relatively late symptom. More usually a rising pulse with a feeling of discomfort, scanty urine, a slight fullness in the hypochondrium, and the obliteration of the normal sulcus immediately beneath the costal margin were very suggestive, and the mere possibility of this should be followed by the passage through the nose of a nasal tube, the aspiration by a glass syringe, attached to the nasal tube (see Fig. 25) of a quantity of dark fluid pointed definitely to the presence of at least some dilatation of the stomach. The principles of treatment were (i) to empty the stomach and to keep it empty. The tube should firstly be placed in ice-cold water. The end is then passed down the nose and made to enter the nasopharynx. The patient is then given sips of water, and with each gulp the tube is passed onwards until it is well within the stomach, (ii) to give continuous intravenous saline, and (iii) to invoke the aid of gravity; with the gastric aspiration tube *in situ* the stomach can be emptied and kept empty, but posture, which was formerly

given a high place, was of secondary importance. The high Trendelenburg position, though not employed by the author, we think it would be more generally applicable than the prone posture with elevation of the foot of the bed. Pserine 2.00 grain injected at four-hourly intervals for 3 doses was useful, in combination with the gastric aspiration tube *in situ*, in keeping the stomach empty. It was more than probable that primary or delayed shock, particularly in patients in the Fowler position, might favour gastric dilatation, but this could not be the complete explanation, and the initial factor is unknown.

Bailey, H. (1939) *Brit. med. J.*, **1**, 434.

Mycotic Infections

C. Bearse pointed out that the diagnosis of mycotic infections of the stomach might prove difficult because there were no characteristic symptoms. The complaints were similar to those in functional dyspepsia or peptic ulcer. When fungi were found in the vomitus, and this finding was confirmed in uncontaminated gastric contents, growth of a culture was attempted. If the inoculation of this culture into a rabbit gave a typical reaction and was corroborated by positive blood cultures, intradermal tests and blood agglutinations, a diagnosis of mycotic infection was made. The gastroscope was often very useful in diagnosis. In actinomycotic lesions in which there was a sinus, a diagnosis was made from the sinus curettings, which disclosed ray fungi. In this case the possibility of metastases in the liver must be kept in mind. Treatment consisted in administration of iodides to the point of tolerance, when actinomycotic sinuses were present, X-ray treatment was used, and when perforation or repeated haemorrhages occurred, operations were necessary.

Bearse, C. (1938) *Amer. J. digest Dis.*, **5**, 674.

Effects of Tobacco Smoking

The effects of tobacco smoking on the alimentary tract were studied by J. G. Schnedorf and A. C. Ivy. It stimulates the flow of saliva in almost every subject. It inhibits hunger contractions through a reflex mechanism. It does not delay the emptying of a test meal from the stomach but in some cases may inhibit gastric evacuation and secretion. It does not tend to cause significant gastric retention nor, contrary to the view of many, does it increase the acidity of the stomach. In the absence of marked fluctuations of blood pressure the secretion of biliary and pancreatic juice is unchanged. Smoking encourages the motor activity of the colon.

Schnedorf, J. G., and Ivy, A. C. (1939) *J. Amer. med. Ass.*, **112**, 898.

STRABISMUS

See also Vol. XI, p. 492, and p. 131 of this volume.

Aetiology

J. N. Novick reported two cases of diplopia following Caldwell-Luc operations, due to injury and subsequent paralysis of the inferior oblique muscle. In both cases the diplopia disappeared spontaneously after a few days.

Novick, J. N. (1938) *Arch. Otolaryng., Chicago*, **28**, 412.

STURGE'S DISEASE

A case of Sturge's disease, bringing the total of recorded cases to 145, was described by A. M. Nussey and H. H. Miller. The main abnormalities seen in this congenital, and perhaps hereditary, condition were: (i) A cavernous naevus of a port-wine colour in the distribution of one or more branches of the trigeminal nerve. The overlying skin might hypertrophy. (ii) Vascular changes in the eye of the same side, with glaucoma and exophthalmos in one third of the cases. (iii) Changes in the pia varying from a slight telangiectasis to a racemose venous angioma. (iv) Marked cerebral changes, namely hypoplasia, atrophy, and calcification confined to one side of the cerebrum. The calcification was partly perivascular and partly a deposit of free calcium granules in the brain. The symptoms of cerebral affections arose early in life, often before the age of 10, and consisted of either focal or generalized epileptiform

seizures, hemiplegia, hemiatrophy after the injury, the degree of amentia. The commonest site of calcification was the occipital region. On screen examination, the shadows thrown by the calcium in the cornua were sinuous, and when the X-rays struck a sulcus at a right angle, two lines running 2 mm. apart could be seen. The immediate prognosis was good, but, in the more severe forms, mental degeneration must be expected subsequently. Attempted removal of diseased cerebral areas, ligation of the common carotid artery, and decompression had given poor results. X-rays or radium therapy had been beneficial.

Nussey, A. M., and Miller, H. H. (1939) *Brit. med. J.*, **1**, 822

SYMPATHETIC AND PARASYMPATHETIC NERVOUS SYSTEM

See also Vol. XI, p. 503, and p. 121 of this volume.

Physiology

Action of Drugs and Hormones

The active substance liberated by cholinergic nerves is acetylcholine, but the substance liberated by the adrenergic nerves has not yet been identified with certainty. The demonstration of acetylcholine as the substance liberated depends on the action of eserine which inhibits the hydrolysis of acetylcholine by choline esterase. J. H. Gaddum and H. Kwiatkowski investigated the suggestion that ephedrine might protect adrenaline in the same way, if adrenaline is the substance produced by the adrenergic nerves, probably by destroying amine oxide which may be the substance which destroys the adrenaline. They found that stimulation of the sympathetic nerves of the rabbit's ear which had been perfused with ephedrine produced vasoconstriction and the liberation of a substance which can be detected by a colorimetric test for adrenaline. Low concentrations of ephedrine sensitize the rabbit's ear, the cat's nictitating membrane, and the frog's heart not only to adrenaline but also to the stimulation of adrenergic nerves. The action of ephedrine also increased the amount of substance liberated by the adrenergic nerves so that its properties could be studied. It was found not to be noradrenaline, epinine, corbasil, or adrenaline, but it may possibly be adrenaline.

Gaddum, J. H., and Kwiatkowski, H. (1938) *J. Physiol.*, **94**, 87.

Renal Sympathetico-Tonus

A. C. Abbot and F. Stephenson gave a careful description of the nerve supply of the kidneys, and investigated the functional and anatomical changes found in the kidney when the neuromuscular mechanism is in a state of imbalance. This condition is termed by Harris 'renal sympathetico-tonus', and is chiefly found in neurotic, easily tired females. The symptoms include a chronic dull ache in the loin with occasional acute attacks of renal colic, abdominal pain and indigestion, haematuria, and anuria. The affected kidney may be palpable, enlarged, and freely movable. Costovertebral tenderness on percussion and palpation is invariably present and calculi may be found in the advanced stages. Pyeloscopy is regarded as a valuable procedure in diagnosis, if properly carried out, but cystoscopic examination is considered the most certain method. All other morbid processes must be ruled out before diagnosing a renal sympathetico-tonus. The three general reasons for performing sympathectomy are relief of vasomotor spasm, pain, and muscular spasm. All these factors are present in renal sympathetico-tonus. It is essential, before proceeding to surgical denervation, to know that there is one healthy kidney. A series of 10 cases, collected during 13 years, is described.

Abbott, A. C., and Stephenson, E. (1939) *Canad. med. Ass. J.*, **39**, 542.

Clinical Applications of Sympathectomy

E. D. Telford reports on 4 conditions for which he has performed a sympathectomy. He describes the sympathectomy in these cases as pre-ganglionic, i.e. section was performed by dividing white rami before they reached their ganglion cells, a process which the author considers preferable to post-ganglionic section. The vasodilatation causes a bright red flushing of the skin and a rise of temperature

of 8 to 10° C. The immediate effects of sympathectomy were in each case gross flushing and heat of the skin with complete abolition of sweating. The skin temperatures, particularly in the lower extremities, remained above normal, often for many years after the operation. (i) Raynaud's disease: sympathectomy is recommended in severe cases of Raynaud's disease as a prophylactic measure against sclerodactyly. When fibrosis is apparent and sclerodactyly is established, the results from sympathectomy are disappointing, and when contraction and painful ulceration are present, benefit is unlikely to result. Sympathectomy in cases of the patchy and superficial form of scleroderma sometimes brings about improvement. (ii) Hyperhidrosis: excessive sweating may be treated successfully by sympathectomy. The activating fibres run out of the spinal cord with the vasoconstrictors in such close association that operative selection is not possible. Hence every sympathectomy, whilst causing vasodilatation, also destroys the function of sweating. (iii) Erythema induratum: in infantile paralysis, erythrocyanosis, and Bazin's disease, small subcutaneous nodules may form, usually on areas where there is a good deal of fat and poor circulation, and the nodules appear upon exposure to cold. The condition is described as a lipophagous granuloma. The results of lumbar sympathectomy in such cases have been excellent, especially in younger patients. (iv) Trophic ulceration: a case which illustrates the value of sympathectomy in this condition is that of a man who suffered a gunshot wound of the cauda equina, with resulting total paralysis of the right leg below the knee, and ulcer formation over the heads of the fourth and fifth metatarsals, which remained unhealed for 18 years. After a right-sided lumbar sympathectomy, the ulcer healed in 6 weeks. The author considers that, although the operation of sympathectomy is still on trial, it may prove of lasting benefit in selected cases of skin diseases.

Telford, E. D. (1938) *Brit. J. Derm.*, **50**, 637.

SYPHILIS

See also Vol. XI, p. 526, Cumulative Supplement, Key No. 1467, and p. 151 of this volume.

Historical

V. Robinson, in a survey of the history of syphilis, reviews the evidence in favour of the origin of the disease in America. He quotes from Oviedo and Las Casas' *Historia de las Indias* and from the *Tractado contra el mal venetico* by Ruiz Diaz de Isla. It would appear that the Indian inhabitants of Haiti had suffered from syphilis long before the arrival of Columbus and the Pinzons, and to such an extent that the natives seemed to possess a natural immunity to the scourge in so far as severity of symptoms was concerned. Robinson suggested that the sex-starved Spaniards on arrival in the West Indies turned Haiti into a brothel, and the parasite from the genitalia of the Indian women found fresh soil, and thus began the 'syphilization' of the white race. There seems to be some doubt whether the first infected was Christopher Columbus or one of the Pinzon brothers, who accompanied him on the voyage to America.

Robinson, V. (1938) *Brit. J. Derm.*, **50**, 593.

Laboratory Tests

Microscopical

Staining of spirochaetes.—S. O. Chambers and J. R. Scholtz have described a method of staining spirochaetes after biopsy. A solution of 2 to 4 per cent procaine hydrochloride or butyn is used on the edge of the lesion, and a small piece of tissue is removed and placed in 10 per cent formaldehyde solution; it is then stained by Krajian's method. The method has the advantage of quickness, and the apparatus required is present in any consulting room. It has been found to be very efficient, and the stained slide can be kept for future reference. Confusion with saprophytic organisms is eliminated, because they are surface organisms which are not included in the biopsy. The spirochaete is the only organism which retains its morphological characters after death, so that its presence in biopsy material is diagnostic. Diseases due to other spirochaetes are unlikely to occur in the northern hemisphere. It was found that the stain gave 98.8 per cent positive results in syphilitic lesions, whereas

dark-ground illumination gave after the injection. The stain has also been found of use in detecting the spirochaete in the case of erysipelas, in some large cutaneous syphilides, and in material removed at operation and at necropsy.

Identification of spirochaetes in serous smears.—An additional technique for the identification of *Spirochaeta pallida* in fresh serous smears was described by A. A. Krajan. The lesion is rubbed with a swab dipped in alcohol until its surface bleeds. When all bleeding stops, a clear serous exudate appears which is smeared on a slide and dried in air. Each smear is flooded for 5 minutes with a warm solution of uranium nitrate, 1 g.; 85 per cent formic acid, 3 c.cm.; pure glycerin, 5 c.cm.; acetone, 10 c.cm.; and 95 per cent alcohol, 10 c.cm. It is then washed in distilled water and treated with a solution of 3 drops of saturated alcoholic solution of mastic mixed with 7 c.cm. of 95 per cent alcohol, for 2 minutes. The gum is poured off, and breath blown on the surface of the smear, the slide then being washed in distilled water. The slide is flooded with a 1 per cent aqueous solution of silver nitrate, heated over a burner until bubbles begin to form (not boiled) and kept at this temperature for 3 minutes. The silvering is repeated once, then the silver poured off, and a thin coating of developing solution applied, and the slide left under electric light for 2 minutes while warmed gently with a flame. The stained slide appears brown. The developing solution consists of hydroquinone, 0.31 g.; sodium sulphite, 0.06 g.; 40 per cent neutral solution of formaldehyde, 2.5 c.cm.; pyridine, 2.5 c.cm.; saturated solution of mastic in 95 per cent alcohol, 2.5 c.cm.; and distilled water 15 c.cm. The slide is then washed in water, dried with filter paper, and examined. The mastic solution should be prepared freshly, but the developing solution keeps from 2 to 3 weeks in a light room, after which the mastic separates and settles to the bottom of the bottle.

Serum Tests

Kline precipitation test—K. F. Miller has found that the Kline precipitation test in both diagnostic and exclusion procedures is the most reliable and sensitive in the diagnosis of syphilis. If both types of test are negative, reaction to all tests may be considered negative in practically all cases, but when the exclusion test alone gives a doubtful result, the Kline diagnostic and the complement-fixation method (Wassermann) should be used. If, however, a discrepancy persists, the burden of proof is considered to rest with the precipitation test. These observations resulted from the study of 550 cases, in 50 of which the mother was known to have syphilis either from the history, or from tests of her blood during the pre-natal period and puerperium, or of the cord blood and of the baby's blood.

Simplified technique for complement-fixation test—I. Boerner and M. Lukens described a simplified technique for the complement-fixation test for the diagnosis of syphilis. It was cheaper, reduced the chances of error, admitted the inspection of the technician at every stage of the procedure, and was equally applicable to qualitative and quantitative tests. The test differed from any hitherto devised in that certain of the reagents were mixed in bulk. The antigen and complement were combined and added in fixed amounts to the patients' serum, which had already been inspected to see that there was no reduction or excess in any tube. The tubes were then placed in the refrigerator for fixation, when a suspension of previously sensitized erythrocytes was added in fixed amount to each tube. The contents of the tubes could again be inspected. They were then shaken, placed in a water-bath, and the test was made in the usual manner.

Boerner, F., and Lukens, M. (1939) *Amer. J. clin. Path.*, **9**, 13.

Chambers, S. O., and Scholtz, J. R. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 217.

Krajan, A. A. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 427.

Miller, K. F. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 918.

Acquired Syphilis

Prognosis

In connexion with the occurrence of syphilitic infection without any manifestations of the acute stage of the disease, H. J. Morgan argued that the amount of the inoculated material may play a causal part. He agreed with Bruusgaard that approximately 25 to 35 per cent of patients with untreated latent syphilis were ultimately cured clinically, and that an additional 25 to 35 per cent did not show any evidence of infection except a positive Wassermann reaction of the blood. Systematic life

assurance examination had shown that 99.9 per cent of 100,000 applicants, who were favourably considered except for a history of syphilis, the mortality was about 1.4 times the generally accepted mortality. The expectation of life is shortened as compared with that of the general population between the age of 30 and 60 by 17 per cent among white males, and by 30 per cent among negroes. It is higher in women because serious lesions of the central nervous and cardiovascular systems are distinctly less than in males. Untreated syphilis was an extremely serious complication of pregnancy; only 17 per cent of such pregnancies resulted in healthy non-syphilitic offspring who survived infancy. In a series of cases adequate treatment started before the fifth month was followed by the birth of a non-syphilitic child in 91 per cent. The rate of cure for adults in the acute stage was 90 per cent, with a percentage success of 70 to 80 among those with early latent syphilis. The treatment of late latent syphilis was particularly emphasized, because it greatly reduced subsequent morbidity and mortality from cardiovascular and tertiary syphilis.

Tertiary

Syphilitic steatorrhoea and tetany.—J. Caroli *et al.* reported a case of chronic steatorrhoea of syphilitic origin which was complicated by attacks of tetany. This case, one of the very rare manifestations of visceral syphilis, presented many difficulties, and the steatorrhoea was of extreme degree. The patient, who 25 years ago had had a syphilitic lesion of which he was completely cured serologically, lost between 1 and 2 kg. of fatty stools daily, his attacks of tetany were so marked that Chvostek's, Trousseau's, and Lust's signs had to be elicited with extreme caution for fear of provoking more violent convulsions. No treatment was of any avail; the serological tests for syphilis were all negative. At the patient's request, in spite of medical objections, antisymphilitic treatment was carried out months after his last very bad attack and yielded an astonishingly quick successful result. It is considered that most chronic steatorrhoeas are of syphilitic origin.

Caroli, J., Girard, M., and Joanissian, M. (1939) *Bull. Soc. méd. Hôp. Paris*, **55**, 785.

Morgan, H. J. (1939) *J. Amer. med. Ass.*, **112**, 311.

Congenital Syphilis

Diagnosis

Enlargement of inner end of clavicle.—E. C. Dax and R. M. Stewart examined 64 cases of congenital syphilis to verify the claim of Higouménakis that an enlargement of the sternal end of one clavicle, and particularly of its inner third, is an important diagnostic physical sign. Such a sign is not present in acquired syphilis, but may exist in a modified form in a small proportion of non-syphilitic cases (approximately 5 per cent) from rachitic causes. The enlargement is usually of 3 types: (i) a generalized enlargement of the sternal end, (ii) an exostosis projecting from the inner end of the bone; and (iii) a roughening of the inner third. The sign was found in 19 of the 64 cases representing 30 per cent of the series, similar lesions were found in 5.4 per cent of 1,200 non-syphilitic controls. In a small majority of them the enlarged clavicle was on the left side. The development is explained by Higouménakis as a hyperostosis, the sequel to an osteitis.

Dax, E. C., and Stewart, R. M. (1938) *Brit. med. J.*, **1**, 771.

Treatment

Acquired Syphilis

Massive arsenotherapy.—H. T. Hyman *et al.* reported the late results of the treatment of 25 male patients in the primary or early secondary stages of syphilis with massive arsenotherapy by means of an intravenous drip. A total of 100 g. of neoarsphenamine was given in an average time of less than 5 days. There were no toxic signs of heavy arsenotherapy, such as jaundice or exfoliative dermatitis. The results were reviewed 5 years afterwards. Five of the patients disappeared from observation before their serum was negative; in 5 more the serum became negative, but the patients were not followed to ensure that their condition was satisfactory. Of the other 15, 11 have given repeatedly negative results to the Wassermann reaction. The spinal fluids of 13 of this group are also negative. Nine normal tele-roentgenograms were obtained in this group, one at the end of 4, and the others at the end of 5 years' observation. Of the other 4 patients, 2 became reinfected with

syphilis; one disappeared from the injection for 4½ years during which time he was intensively treated with mercurial in cases by a hospital orderly. The remaining patient was still 4+ one month after treatment; he was not seen again for 4½ years, when his blood and cerebrospinal fluid reactions were negative and his tele-roentgenogram was normal. The authors considered that this short treatment of only 4 or 5 days, though still in its experimental stage, is so successful that it may well take a place in the treatment of primary and early secondary syphilis.

Mapharside.—R. V. Rajam, and N. V. Rao used mapharside (*m*-amino-*p*-hydroxyphenylarsine oxide) in a series of 1,000 cases of syphilis. It was found that in 14 out of 15 selected cases after one single dose of 0.04 g. of mapharside a dark-ground examination became negative to *Spirochaeta pallida* within 18 to 24 hours. In 50 cases of primary chancre, the sores healed, on an average, after 2 to 5 injections. Eruptions in 46 cases of secondary syphilis cleared up, on an average, after 3 to 6 injections, and the response of late benign syphilitic lesions was equally satisfactory. Pregnant women were treated with beneficial results. The immediate reactions of mapharside, particularly fever, vomiting, and diarrhoea, seemed to be more frequent than those of neoarsphenamine but were, in the main, mild and transient. Delayed reactions were less frequent than with neoarsphenamine, and no case of exfoliative dermatitis occurred. Two deaths following mapharside therapy are reported, one from encephalitis and the other from granulocytopenia. The stability and non-toxicity in solution of mapharside make it an improvement on the older arsenical trivalent drugs, especially in institutional treatment. The therapeutic unit dose is about one-tenth that of neoarsphenamine preparations.

Congenital Syphilis

Mapharside.—V. A. Cornell and G. D. Astrachan treated 31 cases of late congenital syphilis and 11 cases of early congenital syphilis with intramuscular injections of mapharside. The ages in the combined groups ranged from 2 months to 11 years. The number of injections in any one patient ranged from 4 to 76, the average being 12 in early cases and 24 in late cases. The average dose was 2.5 mg. in early cases and 13 mg. in late cases (extremes 3 mg. and 25 mg.). The injections were given once a week and were accompanied with, or followed by, bismuth injections. Mapharside produces very few toxic symptoms in children, and it proved useful in late congenital syphilides, giving an improvement in more than 50 per cent of cases. Despite the effectiveness of the drug, further experimental work is considered necessary before a definite statement can be made regarding its use in early congenital syphilis.

A case is reported by G. M. Wyatt and B. W. Carey of a 10 weeks' old female admitted to hospital with congenital syphilis with syphilitic meningitis. The symptoms were of 8 weeks' duration. Intravenous injections of mapharside were given after 2 weeks' treatment which consisted of a mercury binder and, later, injections of bismuth, 8 mg. repeated at intervals of 3 days. The symptoms became worse, the condition being aggravated by vomiting, diarrhoea, and pyrexia. Two days after the last injection of bismuth, intravenous mapharside was commenced in a dosage of 0.25 mg. per kg. of body-weight. Given bi-weekly the dose was increased by 0.25 mg. on each occasion to a maximum of 1 mg. per kg., a total of 12 injections being given. Subsequently the bismuth was resumed with injections of 10 mg. intramuscularly for 8 weeks, followed by 12 further weekly injections of mapharside in a dosage of 1.0 mg. per kg. of body-weight. Immediate response to the mapharside treatment was noticeable, and examination of the cerebrospinal fluid showed a drop in the total protein from 258 mg. per 100 c.cm. to 96 mg. per 100 c.cm. and in the total leucocyte count from 440 to 12 mononuclear cells, while the sugar was raised from 20 mg. per 100 c.cm. to 31 mg. per 100 c.cm. Both Wassermann and Hinton blood-tests were positive. The opisthotonos disappeared 3 weeks after the commencement of mapharside treatment. The patient was discharged from hospital but kept under observation. At 6 months of age cortical atrophy was shown by encephalograms, but at 18 months, although the lateral ventricles were still dilated, there was marked increase in the amount of cortical tissue. This child remained continuously under antisymphilitic therapy, and by the age of 25 months satisfactory progress in both mental and physical development had been observed.

Acetarsol.—D. M. Pillsbury and H. H. Perlman administered acetarsone (acetarsol) orally to 187 cases of congenital syphilis, 87 of which were diagnosed within 3 years of the patient's first attendance at the clinic. Although it has been generally accepted that acetarsone is the drug of choice for congenital syphilides, the toxic effects were numerous. Some reactions occurred in 10.7 per cent of the patients

treated. Nephritis occurred in 4.6 per cent. The author emphasizes that its appearance should be taken as a contra-indication for further treatment. Reactions in different classes of experimental animals varied widely, and it was not possible to standardize the toxicity of the drug by animal experimentation. Severe reaction became evident in one patient who developed a generalized dermatitis, hepatic enlargement, paralysis of the left external rectus muscle, and high temperature. Except for this case, skin reactions were slight.

The system of dosage employed was that suggested by Maxwell and Glaser, which commences with small doses of one-quarter of a 0.25 g. tablet (1 grain) once a day for the first week, rising to one tablet twice a day in the sixth week. The author considered, however, that a system of dosage based on weight would be preferable. Cutaneous and muco-cutaneous lesions were healed in 2 to 4 weeks, but generally speaking the effect of acetarsone was slower than that of arsphenamine and approximated more to that of the soluble bismuth compounds. Interstitial keratitis did not respond satisfactorily. It was concluded that there could be no doubt that acetarsone was a valuable spirochaetocide. The fact that it can be administered orally was considered a doubtful advantage as it allowed a latitude for carelessness on the part of irresponsible patients.

Side Effects of Arsphenamine Treatment

Then prevention and treatment. C. Kuehn *et al.* reported 2 fatal cases of arsenical encephalitis due to the treatment of syphilis by arsphenamine during pregnancy. Both occurred in the eighth month of pregnancy, and both were characterized by the onset of rapidly progressive respiratory paralysis. Coma, lateral nystagmus, exaggerated reflexes, and incoherent movement of the extremities were also present. Necropsy demonstrated a haemorrhagic encephalitis. The authors suggested that patients receiving arsenic during pregnancy should be frequently examined and, during the latter half of pregnancy, should receive smaller doses at weekly intervals.

L. Ferrabouc and R. Cadeot discussed the accidents which can occur in the treatment of syphilis and which are due to the action of arsphenamine. The conditions noted included purpura, haematuria, haemorrhages from the digestive tract, and one case of haemorrhagic sialorrhoea. The treatment of these conditions is prevention by slow injection of the drug, a prophylactic injection of adrenaline, dilution of the drug in sodium thiosulphate, and administration of vitamin C as recommended by Dainow. In fully developed cases intramuscular or intravenous injection of adrenaline and injection of posterior pituitary extract are necessary. In grave cases blood transfusion and intravenous calcium are given with good results.

Bismuth

Jaundice.—R. Nomland *et al.* studied 32 cases of bismuth jaundice occurring among 75 cases of jaundice resulting from antisyphilitic treatment. Some other causes of jaundice in this group were arsphenamine, tryparsamide, and mercury. The criteria for diagnosis were lack of evidence of liver or biliary disease, development of the jaundice within a reasonable time after the last treatment (in the case of bismuth 6 weeks), and complete clinical recovery. Twenty-two of the patients with bismuth jaundice had also received neoarsphenamine but not within 12 weeks of the onset of the jaundice. The amount of bismuth given in 9 cases was 11 to 20 injections, in 6 cases from 21 to 30 injections, and in 5 over 30 injections. The other 10 patients developed the jaundice within 1 to 3 weeks of the last treatment. In all cases a 10 per cent suspension of bismuth salicylate in doses of 1.5 to 2 c.cm. per week had been given. Clinically the jaundice was indistinguishable from other forms of toxic jaundice, and all the patients recovered. In 6 of the patients the jaundice lasted for 6 weeks, but many of the group received bismuth after their recovery and no ill effects resulted.

Cornell, V. A., and Astrachan, G. D. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 943.

Ferrabouc, L., and Cadeot, R. (1939) *Rev. méd. franç.*, **24**, 259.

Hymen, H. T., Chargin, L., and Leifer, W. (1939) *Amer. J. med. Sci.*, **197**, 480.

Kuehn, C., Keating, R. A., and von Haam, E. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 122.

Nomland, R., Skolnik, E. A., and McLellan, L. L. (1938) *J. Amer. med. Ass.*, **111**, 19.

- Pillsbury, D. M., and Perlman, the injec (1939) *Arch. Derm Syph., N.Y.*,
 39, 969
 Rajam, R. V., and Rao, N. V. (1939) *Indian med Gaz.*, 74, 24.
 Wyatt, G. M., and Carey, B. W. (1939) *Amer. J. Roentgenol.*, 41, 779.

TALIPES

See also Vol. XI, p. 628

Congenital Talipes

Treatment

Adhesive plaster method. K. Gaugele stated that it should be possible to treat every case of congenital talipes with satisfactory results. The old treatment of talipes consisted of plaster of Paris bandages or surgical boots and gave most unsatisfactory results owing to delay in treatment until the sixth month or end of the first year of life. The modern treatment consists in the application of an adhesive plaster bandage soon after birth (seventh or eighth day). A strip of adhesive plaster (6 to 8 cm wide) is fixed at the outer border of the foot, wound round the foot, and from the outer border up to and round the thigh, the knee being bent at a right angle; from that point it is brought down and around the anterior part of the leg. A second layer is fixed in the same way. Constant examination (every half-hour) is necessary to prevent the bandage from causing swelling or cutting into the flesh. It takes between 6 and 8 weeks to get the feet into a straight position. The plaster is then replaced by metal splints. Exercises are very important. In older children, operation is still the only means of treating talipes.

Gaugele, K. (1939) *Med Klinik*, 45, 310

TAPEWORM INFECTIONS, INTESTINAL

See also Vol. XI, p. 642.

Diphyllobothrium Latum

Influence on Gastric Juice

B von Bonsdorff examined the possible relation between anaemia due to intestinal worms and the components of the gastric juice, notably Castle's intrinsic factor. Previous workers affirmed that intestinal parasites inhibited the proteolytic activity of trypsin, papain, and pepsin. The author's extensive and careful experiments with aqueous extracts of fresh and dried *Diphyllobothrium latum*, *Taenia saginata*, and *Ascaris lumbricoides* have shown an inhibitory influence on the proteolytic action of normal human gastric juice, but no such action was noticeable on the trypsin, papain, and pepsin of highly acid gastric juice. The worm proteins were quickly digested by trypsin, papain, and pepsin, but not by neutral gastric juice. *Diphyllobothrium latum* was found to have a marked proteolytic action on casein, with a maximum at pH 4. The enzymatic activity of *Taenia saginata* and *Ascaris* was not so marked.

Treatment

Liver extract.—B von Bonsdorff, examining the effect of the presence of *Diphyllobothrium latum* on liver extract, conclusively showed that the presence of the worms in the intestines made no difference to the efficacy of the liver extract employed in treating the pernicious type of anaemia sometimes present in this infestation.

Bonsdorff, B. von (1939) *Acta med scand.*, 100, 436.

— (1939) *ibid.*, 100, 459.

Tapeworm Infections Generally

Treatment

Atropine sulphate.—R. Wigand emphasized the importance of relieving muscular spasm in the intestines when treating intestinal worms. In his view failure to evacuate the scolex is due to muscular spasm in the wall of the intestine. He therefore administered as a routine 1 to 2 hours before starting treatment, 1 mg. of atropine sulphate

subcutaneously (for children the dose is proportionately reduced). He obtained a more rapid result and no failures with this procedure.

Wigand, R. (1939) *Dtsch. med. Wschr.*, **65**, 923.

TESTIS AND CORD DISEASES

See also Vol. XI, p. 656.

Tumours

Morbid Anatomy

A. U. Desjardins insists that primary malignant tumours of the testes produce secondary growths much earlier than is generally recognized in the upper para-aortic lymphatic glands, and never give rise to involvement of the inguinal lymphatic glands unless the testicular tumour has perforated the capsule of the testis.

Chorionepithelioma.—S. McDonald, Jr., reported a case of chorionepithelioma of the testis in a gas-fitter, aged 24, characterized by enlargement of the testis, exophthalmos, slight gynaecomastia and reddish-brown pigmentation around the nipples, subcutaneous metastasis on the right shoulder, and a positive Aschheim-Zondek reaction. Necropsy showed some enlargement of the thyroid, and metastases in the brain, spine, liver, kidneys, lungs, skin of the right shoulder, and retroperitoneally. The patient died of a terminal acute nephritis and lobar pneumonia. The tumour was morphologically identical with uterine chorionepithelioma, though it was believed to arise from the malignant differentiation of a testicular teratoma. The recorded cases, the nature of the growth, and the Aschheim-Zondek reaction (presence of luteinizing and follicular-stimulating hormones in the urine) and the diagnosis by this means from other testicular tumours, especially seminomas, were discussed. A quantitative estimation of the gonadotrophic hormones in the urine should be an essential procedure in the investigation of all testicular tumours, and correlation of the amount of urinary gonadotrophic hormones with the histology of the tumour might afford valuable information about the nature and source of gonadotrophic hormones, whether from the pituitary and hypothalamus or from the chorionic villi of the placenta. At present the reports of a negative Aschheim-Zondek reaction in undoubted chorionepithelioma should be regarded with reserve.

Prognosis

Survival rates in malignant disease.—H. Cabot and J. Berkson followed up 98 per cent of 363 patients seen at the Mayo Clinic between January 1st, 1910, and January 1st, 1937, of these there were 148 who were entirely diagnosed and treated at the Clinic, whereas the remaining 215 were diagnosed, and in many instances treated elsewhere. Out of the 148 patients complete details, including orchidectomy, were available in 142, and these were analysed. The recorded survival rate after orchidectomy for malignant disease was much more favourable than that usually stated. Thus, among the seminoma cases the survival rates for 5 and 10 years were 68 and 47 per cent, the patients irradiated showed survival rates of 71 and 48 per cent. Among the cases of carcinoma the survival rates for 5 and 10 years were 29 and 27 per cent, those irradiated showing survival rates of 24 and 26 per cent for the 2 periods, and those not irradiated 42 and 27 per cent. The higher rate of survival among those not irradiated was attributable to the presence in the cases treated by irradiation of massive metastases. It was emphatically stated, however, that there was not any evidence in either seminomas or carcinomas of prolongation of life at 10 or more years by irradiation. In cases of seminoma with metastases at the time of orchidectomy, the survival rate was 43 and 37.5 per cent at the 5 and 10 year periods. Analysis of the cases to show what influence the known duration of the disease before operation exerted on the survival rate, showed a slightly higher survival rate at all the periods for patients seen within 1 year of the appearance of the lesion, but the difference was not very significant. In the seminoma cases there was not any clear evidence that early diagnosis affected the outcome one way or the other.

H. Cabot and J. Berkson, in continuation of their statistical analysis of primary malignant tumours of the testis, considered the prognosis for patients who at the time of treatment were known to have massive metastases; these, being the most unfavourable group of cases, should therefore demonstrate most clearly the effect

of irradiation. Out of 73 such patients 49 were treated by irradiation alone, and only 17 per cent survived 3 years and 5 per cent 5 years. In the group of 26 patients on whom orchidectomy, followed by irradiation, was carried out at the Mayo Clinic, 38.5 per cent survived 3 years, 32 per cent 5 years, and 26.7 per cent for 10 or more years.

Treatment

X-irradiation. —F. T. Leddy and A. U. Desjardins dealt with 314 cases of malignant tumours of the testis treated at the Mayo Clinic. Early metastasis had occurred in the para-aortic nodes in 180. The nodes affected were generally those in the vicinity of the coeliac axis, and usually on the same side as the testicular tumour. This spread usually precedes metastases in the supraclavicular nodes and lungs. The abdomen is usually treated through 4 anterior fields, extending from the xiphoid to the pubes, one field being irradiated through each of the abdominal quadrants and through 4 posterior fields at corresponding levels. In addition, the left supraclavicular space is irradiated and also the mediastinum, even though radiography of the thorax may not indicate metastasis. The X-rays are generated at 135 kv. and filtered through 6 mm. of aluminium. Each field receives a dose of approximately 550 r. The treatment is extended over 8 to 16 or more days, depending on the patient's tolerance, as checked by blood counts. The treatment is repeated after an interval of a month. The most important factors influencing prognosis are the type of the tumour and the presence or absence of metastases at the time of treatment. A patient without metastases has about a 60 per cent chance of surviving for 5 years or longer; with metastases, his chances of 5 years' survival are about 30 per cent.

Cabot, H., and Berkson, J. (1939) *Proc. Mayo Clin.*, **14**, 333.

— (1939) *ibid.*, **14**, 337.

— (1939) *New Engl. J. Med.*, **220**, 192.

Desjardins, A. U. (1939) *Arch. Surg.*, **38**, 714.

Leddy, E. T., and Desjardins, A. U. (1938) *Radiology*, **31**, 293.

McDonald, S., Jr. (1938) *Amer. J. Cancer*, **34**, 1.

Hydrocele

Treatment

Sclerotherapy. —C. Fivoli collected the literature on the sclerosing therapy of hydrocele, and reported his own clinical experience. He emphasized that only so-called essential or idiopathic hydroceles should be treated by the injection method. Two to 6 c.cm. of 30 per cent quinine urethane solution were employed, and the patients tolerated the injection very well. In most cases one injection was sufficient, but in a few 2 were necessary. The author recommended substitution of this cheap and rapid method for cases in which operation was not necessary.

A. H. Milbert treated 26 patients for hydrocele and spermatocele by the aspiration and sclerosing method, using a combined solution of quinine hydrochloride 5.5 per cent, urethane 3 per cent, and diothane 0.75 per cent. The last-named is a phenyl urethane and possesses prolonged anaesthetic action, besides enhancing the effect of the solution. No evidence of idiosyncrasy or toxicity was obtained. Treatment by this means gave promising results, and no infection or reaction was noted in any case. The number of injections ranged from 1 to 5, the majority of cases requiring only one. The author has since concluded that the number may be lessened by allowing an interval of at least 3 weeks between injections, as little would appear to be gained by repeated injections at too-frequent intervals. The dosage was regulated by the amount of fluid aspirated, which ranged from 4 to 300 c.cm.; the appropriate dosage was considered to be from 0.75 c.cm. to 10 c.cm. In addition to the recognized advantages of injection therapy the technique and solution employed by the author were painless; this fact is corroborated by Kilbourne, who treated 28 cases similarly.

Surgical. —M. Wolf has devised a new radical technique for repair of hydrocele which, it is reported, eliminates the induration and swelling often found in these cases. The process consists of freeing only the anterior half or two-thirds of the sac, without detaching the gubernaculum. After evacuation of the contents, interrupted interlocking figure-of-eight sutures are placed round the edges, and act as haemostatic agents. The dartos and skin are closed with a continuous running suture. For an anaesthetic, preference is given to an epidural injection of 2 per cent novocain (procaine hydrochloride) solution. In uncomplicated cases a medium-sized suspen-

sory bandage may be applied, and patients allowed out of bed, and discharged from hospital in 36 to 72 hours after operation.

Fivoli, C. (1939) *Policlinico*, **46**, 1002.

Milbert, A. H. (1939) *Amer. J. Surg.*, **44**, 587.

Wolf, M. (1939) *Surg. Gynec. Obstet.*, **68**, 236.

TESTIS, UNDESCENDED

See also Vol. XI, p. 671, and Cumulative Supplement, Key No. 1480.

Treatment

R. E. Smith believes that it is safe to rely upon the spontaneous descent of undescended testes at puberty in certain cases, although surgical treatment and gonadotrophic therapy have both had a high percentage of cures. In 24 cases he found that spontaneous descent at puberty occurs in all types of undescended testes whether unilateral or bilateral except those associated with herniae, that when descent does take place the testis develops normally; and that at puberty or immediately afterwards there is an increase of the gonadotrophic hormone in circulation. For these reasons he advocated the postponement of surgery and hormone therapy in certain cases until after puberty.

C. E. Rea stated that endocrine imbalance is probably one of the factors in failure of testicular descent, though the actual cause is unknown. The undescended testis resembles the normal till puberty, after which time it degenerates. Nevertheless spermatogenesis may persist into adult life and the author has found living spermatozoa in smears from abdominal testes of guinea-pigs. Probably about 10 per cent of untreated human cryptorchids remain fertile. Experimentally, both in man and pigs, the fixing of the immature retained testis in the scrotum results in active spermatozoa in the semen in 82 per cent of cases. Proof is still lacking that the undescended testis, forced down by gonadotrophic hormones, will mature normally. Failure of the testis to descend should not be considered as a precancerous condition. Treatment of the undescended testis may be deferred until the ninth to the eleventh year. If 6 months' treatment with gonadotrophic hormone fails, orchidopexy should be performed. Obstruction to the seminal ducts does not result in permanent testicular degeneration.

Gonadotrophic Substance

According to W. O. Thompson and N. J. Hackel the effect of the anterior pituitary-like principle from the urine of pregnant women in the treatment of undescended testis is exaggerated. In 38 patients of all ages, they found that descent was produced in only 20 per cent of cases as compared with the average of 61 per cent of reported successes. In patients under 16 years of age, descent was produced in 27 per cent. Descent did not occur in any instance in which the testis was intra-abdominal or deflected over the external oblique muscle. It was concluded that in most cases of true undescended testis, operative procedures were still necessary because mechanical factors prevented descent. But when the testis did not descend, hormonal treatment might facilitate subsequent operative procedures by enlarging the parts involved.

On the other hand, A. W. Spence and F. F. Scowen consider that intramuscular injections of gonadotrophic hormone extracted from the urine of pregnant women should be employed in children in whom retention of the testis does not appear to be due to an anatomical abnormality. The dose employed by them in most patients was 500 rat units injected intramuscularly twice a week, but in older subjects doses as high as 1,000 to 1,500 units have been necessary. Treatment should not be employed in patients under 10 years of age for fear of stimulating a precocious puberty, and the optimal age for treatment is between 10 and 14. The treatment of patients over 18 is unsuccessful, probably owing to an anatomical abnormality. All cases of retractile testes will respond to hormone therapy within 3 months. This active treatment, however, is unnecessary as the testes descend spontaneously before or at puberty. Testes which are situated in the inguinal canal and are mobile, but which cannot be manipulated into the scrotum, will probably respond to hormone therapy. Successes claimed for testes situated in the inguinal canal are 76 per cent when the condition is bilateral and 64 per cent when it is

unilateral. A successful result is more frequent in bilateral (69 per cent) than in unilateral retention (56 per cent), the smaller percentage in unilateral cases being due probably to the greater likelihood of anatomical abnormality. A successful result is unlikely if the retained testis is impalpable or not freely mobile. In those cases of retained testes which respond, a successful result will be obtained within 6 to 9 months. Should there be no improvement within that period, the patient should be subjected to operation as an anatomical abnormality is probably responsible for failure to descend. Prognosis is not affected by genital hypoplasia, hypopituitarism, or inguinal hernia. In patients of suitable age, there are no serious dangers associated with treatment. Undue penile enlargement is unusual and the continued administration of gonadotrophic hormone does not cause testicular degeneration.

Implantation of Pituitary

P. Lombard and G. Gros described a case of undescended testes in a boy aged 12 years who was treated by implantation of the pituitary of a healthy ox. Under local anaesthesia the tibia was exposed and a groove cut into it, into which the gland was deposited. Healing was by first intention, the testes descended within a few weeks and the condition did not recur. The authors pointed out that this was only the first case in a series of experiments and that further communications will follow.

Lombard, P., and Gros, G. (1939) *Mém. Acad. Chir.*, **65**, 735.

Rea, C. E. (1939) *Arch. Surg.*, **38**, 1054.

Smith, R. E. (1939) *Arch. Dis. Childh.*, **14**, 1.

Spence, A. W., and Scowen, E. I. (1938) *Lancet*, **2**, 983.

Thompson, W. O., and Hackel, N. J. (1939) *J. Amer. med. Ass.*, **112**, 397.

TETANUS

See also Vol. XII, p. 1

Treatment

Prophylactic

Sulphonamide drugs. R. L. Mayer published a preliminary note on the experimental production of antitetanic prophylaxis in mice by the sulphonamide derivatives, sulphanilamide and 2-sulphanilylamino-pyridine (M & B 693). Mice injected with earth containing tetanus bacilli in suspension usually died with tetanus 3 or 4 days later; of 30 mice, 1, or 3.5 per cent, recovered. Out of 95 mice to which the sulphonamide derivative was given by mouth at the same time as the injection of tetanus bacilli, 41, or 43 per cent, escaped tetanus. Of the 2 sulphonamide derivatives, the second (M & B 693) had the advantage that though less potent it was less toxic.

Anatoxin.—G. Ramon drew attention to the complete success which has attended the use in France of active prophylaxis against tetanus in humans and in domestic animals. The method, first tried in 1923 and used ever since, was based on the use of tetanus anatoxin by subcutaneous administration. The technique evolved in the last 10 years, which has been found completely satisfactory, was the subcutaneous injection at intervals of 2, or preferably 3, weeks of 1, 2, and 2 c cm. of anatoxin. A final dose of 2 c cm. one year later was recommended to ensure complete and durable immunity. This method was of the greatest importance for communities of people, such as soldiers, school children, and miners, in whom tetanus might occur; by its use tetanus is completely banned. Moreover, the French army has vaccinated its horses for 10 years, with the result that there has been no further case of horse-tetanus in France. Another advantage of the method is that it can be given together with antidiphtheritic or other vaccines.

Curative

Antitoxin.—R. Scheidt reported 2 cases of tetanus which developed in persons who had sustained no injury whatsoever, and who, in the course of their work, only came in contact with tetanus bacilli. In these cases the dry toxin must have entered the system by inhalation through the nasal and upper respiratory mucosa. The incubation period was very short, only a few days in both cases, and trismus and other classical symptoms were present. Large doses of antitoxin (40,000 units in

1 case and 100,000 units in the other (50% daily) improved and finally cured the condition.

Mayer, R. L. (1938) *Bull. Acad. Méd. Paris*, **120**, 277.

Ramon, G. (1939) *Pr. méd.*, **47**, 877.

Scheidt, R. (1939) *Munch. med. Wschr.*, **86**, 959.

TONSILS DISEASES

See also Vol. XII, p. 40.

Physiology

Vitamin C Content

H. H. Meyer published his experimental results on the variation of the vitamin C content of human tonsils. The tonsils are important in the defence against infection, and vitamin C also plays an important part in combating infections. He found that the vitamin C content of tonsils is slightly greater than that of other organs. The content in vitamin C is greatly diminished in disease. Tonsils containing normal amounts of vitamin C inhibited the growth of streptococci and pneumococci. Vitamin C is synthesized in the human tonsil from glucose, maltose, or saccharose.

Meyer, H. H. (1939) *Klin. Wschr.*, **18**, 704.

Tuberculosis of the Tonsils

I. R. Long *et al.* examined microscopically 2,000 unselected pairs of tonsils, and reviewed the subject of tonsillar tuberculosis. As it is now recognized that many, if not most, patients with open pulmonary tuberculosis also show tuberculous infection of the tonsils, it is clear that the incidence of tonsillar tuberculosis in a population group including many persons with open tuberculosis would be excessive. Conversely a slight error would be introduced if those with open tuberculosis of the lungs were excluded, because persons with open tuberculosis make up a certain proportion of the population. This investigation was undertaken in the hope that examination of a large number of tonsils removed from children in regions with high tuberculous morbidity and bad hygienic conditions might throw light on the questions (a) whether or not the small tubercles often seen in the tonsils in the absence of demonstrable pulmonary tuberculosis represent primary, or at least exogenous, tuberculosis, and (b) whether or not the tonsillar tuberculosis so frequent in the presence of pulmonary tuberculosis is haematogenous or derived from infected sputum. The material examined was obtained as follows: 1,000 pairs of tonsils from various Indian reservations known to have a high tuberculous morbidity, 600 pairs from Puerto Rico where the mortality-rate, though notoriously high, is much lower than the rates believed to prevail in most Indian reservations, and 400 pairs from Philadelphia where the mortality from tuberculosis is only slightly higher than in the United States as a whole. Of the 2,000 pairs, tuberculosis was found in 81, namely, 6.5 per cent of the tonsils from the Indian reservations, 2.5 per cent of those from Puerto Rico, and 0.25 per cent of those from Philadelphia. Radiograms were available in 35 of the 81 cases, 16 of these showed active tuberculosis of the adult type and 2 active tuberculosis of the childhood type, and in general the tonsillar lesions were cryptic and more extensive than in the remainder of the 35 cases. All stages of regression of tonsillar tuberculosis from active fibroplastic disease to scars indistinguishable from scars of other origin were seen. The relatively massive tuberculosis of the tonsils in pulmonary tuberculosis, its tendency to be bilateral and its chronicity point to repeated infection. As small tubercles tend to regress, it is probable that at one time or another in their course the great majority, if not all, of patients with progressive pulmonary tuberculosis have tonsillar tuberculosis.

Long, E. R., Seibert, M. V., and Gonzalez, L. M. (1939) *Arch. intern. Med.*, **63**, 609.

Tumours

Papilloma

Tumours of the tonsil are rare, benign tumours being even rarer than malignant. Of the benign tumours fibromas are by far the commonest. I. Frank reported

3 cases of papilloma of the tonsil which appeared as light grey or greyish-white pedunculated tumours with rough granular surfaces, the whole having a cauliflower aspect. They were treated by tonsillectomy; histological examination showed the presence of the papilloma but no signs of inflammation. The growth may be sessile or infiltrating.

Frank, I. (1938) *Ann. Otol., etc., St. Louis*, **47**, 715.

Removal of Tonsils

Haemorrhages after Tonsillectomy

In a paper on haemorrhage after tonsillectomy D. W. Ashcroft dealt with (i) factors influencing its occurrence, and (ii) forms of haemorrhage and their management.

(i) Recent acute local infections, such as severe tonsillitis, peritonsillar abscess, sinusitis, and a common cold, increase the risk of haemorrhage during and after operation, and tonsillectomy should be postponed for 4 weeks in children and for 6 weeks in adults. The previous history should bring out evidence of the haemorrhagic state, jaundice was a contra-indication; the operation should be avoided, if possible, just before and during the first few days of menstruation on account of its psychological upset and the delayed coagulation time of the blood. To illustrate the effect of operative measures the statistics furnished by McNally (1927) to the effect that severe haemorrhage occurred in 2.6 per cent of the guillotine cases and 0.7 per cent of the cases in which the tonsils were dissected out, were quoted, and it was emphasized that whichever method was adopted the tonsillar fossae must be dry before the patient leaves the operating theatre. As regards post-operative care no hot fluid or food should be taken during the first 24 hours, hot baths should be avoided for 10 days and there should be abstinence from alcohol.

(ii) Haemorrhage was divisible into 3 types. (a) reactionary, occurring within the first 24 hours after operation. An injection of morphine ($\frac{1}{4}$ grain) should be given and the tonsillar fossae inspected half an hour later. If this measure fails, a pledget of cotton-wool soaked in hydrogen peroxide solution and wrung nearly dry should be inserted into the tonsillar fossa. After a minute the wool is removed and another similar pledget applied in the same manner as the first. Alternatively wool dipped in 1 in 1,000 adrenaline hydrochloride may be employed. If these remedies also fail the patient must be taken back to the operating theatre. Here anaesthesia is induced with 'open' ether and, the mouth having been opened by a gag, single bleeding points are clamped and ligatured. It may be necessary to under-run a bleeding vessel with a catgut stitch threaded on a small curved needle. A swab soaked in iced acriflavine solution 1 in 1,000 is inserted into the fossa and held for 3 minutes. The most advanced measure is the suturing together of the faucial pillars over a gauze plug or gauze-covered pledget of wool. Two sutures suffice, they and the wool are removed after 24 hours. (b) Haemorrhage during convalescence commonly occurred on the fifth night after operation and is associated with the aseptic separation of the primary slough from the bed of the tonsillar fossa. It usually ceased after a hydrogen peroxide gargle. (c) True secondary haemorrhage differed from the previous form in being associated with damage to the muscular tissue in the bed of the tonsillar fossa, and sloughing of the wall of an artery, and was rarer. When this serious complication occurs there is often a small 'warning' haemorrhage followed by a larger one in 24 hours. This usually necessitates transfer to the theatre and the re-employment of the haemostatic measures mentioned above. Suture of the faucial pillars may be necessary. Ligature of the external carotid artery is of doubtful value.

Lung Complications

Lung complications following tonsillectomy are supposed to arise in one of three ways, namely. (i) infection through the cardiovascular apparatus (septic emboli); (ii) aspiration of septic material into the lower air passages; and (iii) lymphatic infection. The first rests on theoretical and experimental evidence and the third is not favoured by many to-day. The second depends on the assumption that, in the anaesthetized patient in whom the cough reflex is abolished, blood and pharyngeal secretions can be aspirated into the trachea and bronchi. In a series of 109 cases T. Leegaard found by laryngoscopy after tonsillectomy that only 18 had no trace of blood in the larynx or trachea. He found that blood was more likely to be aspirated by the patient if the mucosa had previously been anaesthetized. After operation the patients were examined laryngoscopically from hour to hour; in most the blood had disappeared in 2 hours, in a few cases after 3 to 6 hours. He then

investigated this problem by radiography of the lungs carried out the day before operation and half an hour afterwards, 1 to 2 c.cm. of 40 per cent iodized oil having been placed in the tonsil bed after the upper pole had been dissected free. In 41 patients in whom the mucosa was anaesthetized the oil appeared in the lungs of 31. In 18 patients in whom the mucosa was not anaesthetized the oil appeared in only 5 cases and only slightly in 4 of these. It was more common on the right than the left, presumably because of the straightness of the bronchus on that side. Five patients were controlled by repeated examination to see how long the oil remained in the lung, only one had an appreciable quantity left after 72 hours. The author also found that tonsillectomy in the recumbent position seemed to prevent this downward oozing after local anaesthesia. But in spite of these observations lung complications were not common. In 1,007 patients operated on in T. Leegaard's clinic only 2 developed mild broncho-pneumonia.

Estimation of Prognosis following Tonsillectomy

F. Kotyza investigated the sedimentation rate of erythrocytes in tonsillectomy. The rate was measured by the Westergren method and compared with that before operation. The blood was taken from an uncompressed vein of the arm, sodium citrate was added and the sedimentation rate measured every quarter of an hour for 2 hours and after 12 and 24 hours. (i) The sedimentation rate before the operation, in 200 cases (72 male and 128 female) the rate was normal in 80 per cent and increased in 20 per cent. The normal rate was taken as 1 to 10 mm. in men and 2 to 13 mm. in women during the first hour. (ii) The rate of sedimentation just after tonsillectomy: the sedimentation rate was not increased until 12 hours after operation, and reached its maximum on the third day after operation. Thereafter the rate slowly fell to normal, the rate of the fall differing in uncomplicated and in complicated (rheumatic) cases. In rheumatic infection and nephritic cases the fall to the normal level took as long as 3 months. In uncomplicated cases the rate was normal after 30 to 40 days. There was a definite connexion between increase in the sedimentation rate and increase of globulin fraction of the serum. (iii) The sedimentation rate after the operation wound had healed: in 123 cases control investigations into the rate of sedimentation could be made for 5 months after operation. In 78 cases, or 61 per cent, the sedimentation rate remained low. All the patients were completely cured of their tonsillar and secondary (rheumatic) symptoms. The fall in the sedimentation rate proved that the symptoms were due to tonsillar infection and that the tonsillectomy was beneficial. Twenty-six patients, or 21 per cent, showed a constant rise in the sedimentation rate, they had either an advanced chronic disease of tonsillar origin, e.g. chronic polyarthritis, chronic glomerulonephritis, or an independent inflammatory disease. In 19 cases, or 16 per cent, the sedimentation rate was normal, i.e. between 1 and 10 mm. per hour. In the cases which were satisfactorily cured the sedimentation rate remained on a constant level after 1 to 2 months, which was the time occupied by recovery after tonsillectomy. In conclusion the sedimentation rate was of great prognostic and diagnostic importance in tonsillectomy cases. The rate should be determined before the operation and at regular intervals after it. A lower rate after 1 to 2 months than before the operation proved that the tonsillectomy was justified and that the focus was really removed. If the rate still remained high after 2 or 3 months there was either a chronic secondary lesion (endocarditis, polyarthritis) which had not been cured by the tonsillectomy, or some other inflammatory disease.

Ashcroft, D. W. (1938) *Brit. med. J.*, **2**, 1079.

Kotyza, F. (1938) *Klin. Wsch.*, **17**, 1764.

Leegaard, T. (1938) *J. Laryng.*, **53**, 499.

McNally, W. J. (1927) *Canad. med. Ass. J.*, **17**, 690.

TOXICOLOGY: HOMICIDAL, SUICIDAL, AND ACCIDENTAL POISONING

See also Vol. XII, p. 59, and Cumulative Supplement, Key Nos. 1491–1527.

Gases

Carbon Monoxide

Uraemia.—R. S. Mach and M. Naville published a case of extrarenal uraemia following poisoning by lighting gas. Clinically, the patient presented nervous

symptoms such as Babinski's reaction and other extrapyramidal signs. The blood nitrogen was unduly high, but there was no oedema or hypertension. It was assumed that the uraemia of this patient was secondary to the cerebral lesion caused by the gas. The author concluded from this case that, in affections of the central nervous system in the course of uraemia, the cerebral condition should not necessarily be considered secondary to the renal syndrome, as there are similar cases on record of uraemia of central origin with or without nephritis.

Treatment of acute poisoning —K. G. Koch successfully treated 2 cases of severe acute carbon monoxide poisoning with repeated blood transfusions. The treatment of severe carbon monoxide poisoning consists of a substitution of carbon monoxide in the blood by oxygen. Respiration of pure oxygen or of oxygen-carbon-dioxide mixture is in many cases quite effective. It has been tried, with less success, to increase the oxygen in the blood by ultra-violet irradiation and by injections of sulphur and of methylene blue, on the supposition that, on reduction to leuco-methylene blue, an oxygen molecule would be transferred to the haemoglobin. The simplest method of introducing oxygen into the blood is by blood transfusion, with preceding venesection. The venesection removes carboxyhaemoglobin and the transfusion (e.g. 400 to 500 c cm.) introduces new oxyhaemoglobin. The treatment is an emergency measure and should be followed by oxygen respiration and use of analeptic drugs. The author describes 2 cases in which blood transfusions (1 and 2 respectively) were the means of saving the patients' life, though unconsciousness persisted for 19 and 48 hours.

Koch, K. G. (1939) *Munch. med. Wschr.*, **86**, 126.

Mach, R. S., and Naville, M. (1939) *Schweiz. med. Wschr.*, **69**, 553.

Synthetic Organic Substances

Salicylates

Sodium salicylate.—L. S. Sell reported a case of salicylate poisoning in an 8-year-old boy, suffering from chronic polyarthritis (Still's disease), who was given 10 gr. of sodium salicylate with 10 gr. of sodium bicarbonate, 4 times a day. After having received 190 gr. of sodium salicylate, the patient developed rapid respirations, increased pulse, excessive perspiration, vomiting, abdominal pain, anxiety, and delirium. Laboratory findings showed that the blood (O_2 -combining power was 36 vols. per cent. The urine contained acetone, 4 plus, acetoacetic acid, 4 plus, glucose, none, albumin, none, and salicylates, 4 plus. Salicylates were discontinued and 10 per cent. intravenous glucose injections with sodium bicarbonate retention enemas were instituted. This was followed by 5 per cent. glucose in physiological saline given subcutaneously. The patient was clinically normal on the second day, and in 4 days the last trace of acetone had disappeared from the urine.

Methyl salicylate.—E. H. Baxter *et al.* reported 2 fatal cases of methyl salicylate poisoning. The first, a negro boy aged 3 years, was admitted to hospital with drowsiness for 5 hours, after having taken 60 c cm. of oil of wintergreen 18 hours previously. The child vomited several times after swallowing the solution and was given castor oil. Put to bed at the usual hour, he became increasingly irritable and restless with a marked rise in the respiratory rate. Later he became very excited, continually throwing his arms about and rolling his eyes. He became quiet and would not respond to questions 5 hours later, but became very active if touched. On admission to hospital, he was acutely ill and in a state of dehydration. The face was pinched and the eyes were sunken. The pupils were contracted and there was definite cyanosis of the lips, fingers, and toes. The lungs were clear and heart sounds normal. The blood count showed a leucocytosis of 20,500. The child was given 250 c.cm. of isotonic sodium lactate intravenously, followed by a continuous intravenous injection of the same material. The stomach was washed out with dilute solution of sodium bicarbonate through a nasal tube. The temperature rose to 102° F., accompanied by profuse perspiration. The pulse and respirations became rapid and death supervened 4 hours after admission. Necropsy showed petechiae on both visceral pleurae, the endocardium, the pericardium, the epicardial surfaces of the heart, and the gastric and jejunal mucosa. The lungs showed early bilateral bronchopneumonia with moderate pulmonary oedema. This was accompanied by a dilatation of the right auricle and ventricle. The liver was grossly hyperaemic, with evidence of parenchymatous degeneration. The epithelium of the renal tubules was in a similar condition. The second case was that of a negro baby aged 18 months. Alkaline

treatment should be started before symptoms of acidosis appear. Oil of wintergreen (and methyl salicylate) sold for use as a counter-irritant should always carry a label indicating its poisonous qualities when taken internally.

Metacetaldehyde

D. R. Lewis *et al.* draw attention to the dangers of poisoning in children by meta fuel tablets. A case report is appended of a boy aged 2½ who swallowed one tablet. In spite of the prompt administration of a large quantity of castor oil by the mother and the washing out of the stomach with sodium bicarbonate by the doctor, convulsions supervened in about 5 hours. After another stomach washout and administration of half a pint of saline rectally, a short period of sleep was followed by the recurrence of convulsions every 10 minutes until midnight when consciousness was lost. Rectal salines were continued but the convulsions returned and became almost continuous. Within a few hours of admission to hospital coma supervened and death resulted in 33 hours. There is no known antidote. Apomorphine hydrochloride 1/16 gr was administered, also chloral hydrate and bromides with abundant fluids, including milk; in addition the stomach was rapidly emptied. At necropsy there was cerebral congestion with minute petechial haemorrhages. The lungs showed areas of collapse and congestion. The stomach was empty but the jejunum and upper ileum contained semi-solid bile-stained material. The contents of the lower part of the ileum consisted of a creamy odourless paste. The liver, which was pale, showed histological evidence of fatty degeneration with zonal necrosis. The authors contend that a public warning should be issued concerning the dangerous qualities of this product, which should be distributed with the utmost care.

Baxter, L. H., Hartwell, R. M., and Reck, L. E. (1938) *J. Amer. med. Ass.*, **111**, 2476.

Lewis, D. R., Madel, G. A., and Drury, J. (1939) *Brit. med. J.*, **1**, 1283.

Sell, L. S. (1939) *Arch. Pediat.*, **56**, 55.

Alkaloids

Stramonium

J. Hughes and J. A. Clark report 2 cases of stramonium poisoning, both of which occurred as a result of drinking tea prepared from the seeds of the Jimson weed. Intense thirst and disturbances of vision sometimes precede the onset of acute symptoms, which include the characteristic dilatation of the pupils, and the dry flushed appearance of the entire skin surface reminiscent of scarlet fever. Further symptoms were delirium, restlessness, tachycardia, choreiform movements of the extremities, and clonic and tonic convulsions. It was noted that poisoning by a tea made from the seeds induced a maniacal picture, whereas the eating of seeds and leaves resulted in a comatose state. The degree of poisoning and the duration of symptoms were determined by the amount of the active weed principles ingested, and also by the sensitivity of the patient to the alkaloids atropine, hyoscyamine, and hyoscyne, all 3 of which are contained in the seeds of this plant.

Prompt treatment should be applied, consisting of lavage of the stomach, either with water or a 4 per cent tannic acid solution; a large dose of magnesium sulphate given by way of the stomach tube; or emetics such as ipecacuanha, mustard, or apomorphine. Three grains of soluble phenobarbitone was the sedative dose employed successfully by the author. Paraldehyde *per rectum* or 25 per cent solution of magnesium sulphate given intramuscularly have been found effective. Morphine is contra-indicated. Pilocarpine has been used, but calculation of dosage was difficult, and care should be exercised in its use for elderly people in whom it may cause pulmonary oedema.

Nicotine

Acute poisoning.—J. P. Price reported a case of fatal acute nicotine poisoning in an 8-year-old negro girl. A dark-coloured fluid was poured down her throat and afterwards identified as 'black leaf', a preparation containing 40 per cent of nicotine sulphate. She soon became nauseated and several hours later developed convulsions and a fever. She was given chloroform and a sedative and she passed into a stupor. Within the next 12 hours she had two more convulsions and the stupor became more pronounced. She was given morphine and admitted to hospital. On admission her temperature was 103° F., pulse rate 120, and respirations were shallow and rapid. The pupils were contracted and the tendon reflexes sluggish. Examination of the

blood showed a polymorphonuclear leucocytosis; the cerebrospinal fluid was under a pressure of 40 mm. of mercury and contained 169 cells per c.mm. The smear and subsequent culture of the fluid were negative for bacteria. In spite of treatment with 10 per cent intravenous dextrose and coramine, the child grew progressively worse and died 72 hours after the administration of the poison. Analysis of the stomach and liver showed the presence of considerable amounts of nicotine sulphate. The case differs from the usual type of nicotine poisoning in that the child lived for as long as 72 hours, and there were signs of meningeal irritation in the cerebrospinal fluid. Price was unable to find elsewhere any mention of this irritation.

Hughes, J., and Clark, J. A. (1939) *J. Amer. med. Ass.*, **112**, 2500.

Price, J. P. (1939) *Amer. J. Dis. Child.*, **57**, 102.

Inorganic and Metallic

Mercury

Acute poisoning - I. M. Rabinowitch reported a case of acute mercurial poisoning: a young female had inserted 2 tablets of mercuric chloride into her vagina. The toxic action was unusually slow; vomiting did not occur until 24 hours after the insertion of the tablets. The vomit contained mercury. Forty-eight hours after the commencement of intensive treatment there was a definite improvement clinically. The blood, however, indicated progressive impairment of renal function. The ultimate recovery was complete. The case is of interest, firstly because the mortality associated with this mode of entry of the poison into the body is extremely high, and secondly because, so far as can be ascertained from the literature, such cases of delayed mercurial poisoning have with few exceptions terminated fatally.

Thallium Sulphate

I. Zeus summarized the modern treatment of poisoning by thallium sulphate. This drug has attained a certain popularity for suicidal purposes and, as it is also used in dermatology for epilation, there are a number of reports of accidental intoxication. Thallium acts on the nervous system, on the digestive tract, and on the heart, liver, and kidney. Treatment by vitamin B₁ and sodium thiosulphate was effective in all cases, the constipation was relieved by magnesium sulphate, and cystitis was treated by chamomile instillations.

Rabinowitch, I. M. (1938) *Canad. med. Ass. J.*, **39**, 429.

Zeus, L. (1939) *Fortschr. Ther.*, **15**, 286.

Cyclic Ureides and Barbituric Acid

Tests for Barbiturates

The development of tests for derivatives of barbituric acid is reviewed by E. J. Delmonico. The colorimetric procedure reported by Koppanyi depends on the appearance of a reddish-violet colour produced by the cobalt ion in the presence of an alkali, in a medium such as chloroform. The reagent used for the test includes a 1 per cent solution of cobaltous acetate in absolute methyl alcohol, and a 5 per cent solution of isopropyl amine in absolute methyl alcohol. The extraction of acidified urine and blood filtrates is made by shaking with 10 volumes of chloroform. The test is made by placing 2 c cm. of the colour-free chloroform into a test-tube, followed by the addition of 0.6 c cm. of the isopropyl amine reagent and 0.1 c cm. of the cobaltous acetate reagent. The characteristic reddish-violet colour is then compared with standards made up in the same manner as the unknown, but containing known amounts of the barbiturate under consideration. The extract is either diluted with chloroform or concentrated over a water-bath, in order to bring the colour reaction within the range of the standards. The method of Brundage and Gruber is a modification of the Koppanyi test. Extraction is based on the principle that activated charcoal will adsorb the barbiturates from aqueous solutions. Diluted specimens of urine or blood filtrates are shaken with activated charcoal which is recovered by filtration. The carbon is then mixed with plaster of Paris and the adsorbed barbituric acid is then extracted from this mixture with a solvent, containing equal parts of ether and petroleum ether. After evaporation of this extract, the barbiturate is dissolved in chloroform to which the cobaltous acetate and the isopropyl amine test is applied. Recovery of from 85 to 90 per cent of the barbiturate is possible with both these methods of extraction. Koppanyi's test can be applied in cases of suspected poisoning from some barbiturate.

Treatment

Picrotoxin.—R. Kohn *et al.* reported 4 cases of barbiturate poisoning, 3 of which were successfully treated by the intravenous injection of picrotoxin. The dose of picrotoxin varied, and one patient received a total of 671 mg. The drug is believed to act by overcoming the cerebral and medullary depression caused by the barbiturate. An intravenous injection of picrotoxin had a latent period of several minutes. The drug is best given in fractional doses. Overdosage leads to convulsions followed by increased depression. This happened in one of Kohn's cases. Once the patient is roused enough to perform movements and to prevent unconscious aspiration of mucus into the lungs, the drug may be given intramuscularly. Other treatment, such as the administration of dextrose and fluids, is also necessary in most cases. There is no evidence that picrotoxin, even in very large doses, is harmful to the body metabolism.

Delmonico, E. J. (1939) *Proc. Mayo Clin.*, **14**, 109.

Kohn, R., Platt, S. S., and Saltman, S. Y. (1938) *J. Amer. med. Ass.*, **111**, 387.

Methyl Alcohol**Acute Poisoning**

F. R. Menne reports on 22 cases of vagrant men who had accidentally consumed concentrated methyl alcohol; 14 of these cases were hospitalized and all died within from 5 minutes to 7 hours after admission. It is emphasized that the dangers of consumption of methyl alcohol are retention by the tissues and slow oxidation into formic acid, which is about 6 times more toxic than the alcohol. It has no selective action and disperses to all tissues but appears to harm by direct action the highly specialized tissues of retina, brain, kidney, and liver. Clinical signs included nervous excitability, intense abdominal pain, rapid respiratory and cardiac action, air-hunger, and dimness of vision.

Necropsy showed minute alterations in the central nervous systems, but on the whole the cellular changes were not marked. The eyes showed marked oedema of the retro-orbital fat. The lungs were uniform in appearance, with marked anterior and marginal emphysema, death having been too rapid to allow the development of more serious lesions. Although all these men were known to be habitual drinkers only one liver showed atrophic cirrhosis. Most of them were remarkably fatty and enlarged. Kidneys were slightly increased in weight, engorged, and firm, but microscopically were in an excellent state of preservation. All the stomachs disclosed superficial necrosis. It was thought that the gastric changes were probably due to the re-excretion of the poison through the stomach and intestines as well as to its direct action, which would explain the recurrent abdominal pains and final paralysis which these cases showed.

Menne, F. R. (1938) *Arch. Path.*, **26**, 77.

Oil of Chenopodium

T. L. Birnberg and C. L. Steinberg report the case of a female child of 2½ years who, following upon treatment with oil of chenopodium for threadworms, exhibited signs of poisoning, commencing with lethargy, staggering gait, vomiting, and finally convulsions, and presenting a clinical picture of severe toxic encephalitis. The child had received two 3-day courses of therapy, with 4 days between, the symptoms appearing on the third day of the second course. The total amount of oil given was 72 minims. After 5 hours of continuous convulsions, forced perivascular (spinal) drainage was instituted. Hypotonic saline (0.40 per cent) was given intravenously at the rate of 250 c.cm. per hour and continued until 1,000 c.cm. had been given in 4 hours. Before commencing treatment 15 c.cm. of cerebrospinal fluid were withdrawn, the needle being left *in situ* and the stylet being withdrawn every half-hour. No increase of pressure was noted. The child made a good recovery. The author advanced Retan's theory that forced perivascular spinal drainage is a 'process which literally "washes out" products of inflammation and toxins from the inflamed spaces', and suggested the possible value of this form of treatment in cerebral disturbances due to other toxic agents.

Birnberg, T. L., and Steinberg, C. L. (1939) *Arch. Pediat.*, **56**, 304.

Chlorinated Hydrocarbons

Carbon Tetrachloride

T. M. Peery reported 3 cases of accidental poisoning by carbon tetrachloride, resulting in death from ingestion of a 'roach poison' which contained a mixture of carbon tetrachloride (25 per cent) and ethylene dichloride (75 per cent) and was mistaken for whisky or alcohol. The patients (two negroes and a negress) showed normal temperatures with increased pulse rate. Their respiration rates were 44, 38, and 24 per minute respectively. The negress had shallow respirations with scattered rhonchi over both lung fields. The respirations were laboured in the case of the elder negro, but in the third case (respirations 24) the lungs were clear. The blood urea nitrogen readings were 44 mg., 63 mg., and 54 mg. per 100 c cm. respectively; creatinine 2.6 mg., 8.4 mg., and 8.2 mg. correspondingly; the figures for sugar were 237 mg., 40 mg., and 82 mg. The survival after ingestion of the poison was 6 to 11 hours, 65 to 70 hours, and 6½ days respectively. The necropsy of the negress, who survived for 6 to 11 hours, showed scattered haemorrhages in the serous coverings of the abdominal viscera, and lungs. Microscopically the viscera, including the liver and kidneys, were normal; the absence of central necrosis in the hepatic lobules was correlated with the short survival period; this death was regarded as an anaesthetic one. In the two other cases the liver showed necrotic changes in the cells in the centre of the lobules and damage in the convoluted tubes of the kidneys, many of the epithelial cells being completely necrotic and densely eosinophilic. In the case which did not prove fatal for 150 hours the liver showed evidence of regeneration. In the other case many of the epithelial cells in the convoluted tubules of the kidneys were completely necrotic and densely eosinophilic; the cells lining Bowman's capsule and covering the glomerular tufts were swollen but not necrotic, and in none of the cases was there definite glomerulo-nephritis. The previously reported cases and the results of experimental poisoning were reviewed, and special attention was directed to cirrhotic changes following the acute hepatic necrosis. From a toxicological point of view carbon tetrachloride is widely used as a general solvent, in the manufacture of chloroform, in chlorinating organic compounds, in electroplating, and fatalities had followed its use in the treatment of hookworm infestation.

Peery, T. M. (1938) *Arch. Path.*, **26**, 923.

TOXICOLOGY: INDUSTRIAL POISONING

See also Vol. XII, p. 127, and Cumulative Supplement, Key Nos. 1528-1540

Phenol

A. Winkler reported a case of phenol poisoning occurring in a worker in a chemical factory, whose eyes were suddenly sprayed with phenol from a container. The skin became brownish-red wherever it had been touched by the fluid; the eyes became hazy, and vision blurred. Though a small quantity only of phenol was involved, it produced transient renal parenchymal damage and haemolysis. The author drew attention to the fact that even small quantities of phenol are able to cause generalized damage. General treatment supplementing local measures should therefore never be omitted.

Winkler, A. (1939) *Klin. Mbl. Augenheilk.*, **102**, 810

Phosphorus

Cutaneous Lesions

R. Klaber described a form of dermatitis characterized by erythema, vesication, and in some cases lichenification resulting from contact with match-boxes and matches. The factor responsible was phosphorus sesquisulphide (P_4S_3), which is rarely present in the safety match, but is an essential constituent of the 'strike anywhere' match. The dermatitis occurs usually in warm weather when the patient is perspiring, but some individuals are peculiarly susceptible. The rash appears on the pocket areas, and on the fingers and hands, and often spreads to the face and eyelids. The irritant substance may reach the skin in 3 ways: (i) by handling the striking surface of a safety-match box if this contains it, (ii) by carrying 'strike anywhere' matches loosely in the pocket, and (iii) by handling the striking surface of a

'strike anywhere' match-box, after moths have been struck on it and therefore some of the substance has been transferred from their heads to its surface.

Klaber, R. (1938) *Brit. J. Derm.*, **50**, 451.

Toxic Gases

Fluorine and its Compounds

H. Kellner reported the results of his investigations on the histopathology of the skeletal system under the influence of continued ingestion of sodium fluoride. It was known that fluorine produced osteomalacia, osteoporosis, and hyperostosis but detailed accounts of the microscopical anatomy of the condition were lacking. Continued administration of fluoride caused disappearance of the original bony structures and in place of lamellated bone, interwoven lines of bone developed. On continued administration periosteal hyperactivity was detected, especially in the mandibles and around the muscular, tendinous, and fascial attachments to bones. There were wide-spread decalcification and excentric hypertrophy of long bones. Fluorine inhibited the effect of phosphatase, and in later stages produced a marked similarity to developmental changes caused by rickets, often simulating rachitic osteosclerosis.

Test for fluorides—A. O. Gettler and L. Ellerbrook described a quick and convenient method of detecting fluorides in as little as 50 g. of normal tissue. The test is a modification of the fluosilicate test. In acute fluoride poisoning the test is positive with as little as one drop of stomach contents or urine. They found that the best quantitative method was the thorium nitrate-alizarin volumetric method. In normal human tissues very small amounts of fluorine were found. On the other hand, teeth and bones contain as much as 0.01 to 0.03 per cent. In fatal cases of fluorine poisoning, the tissue content of fluorine is approximately doubled. Similar results were obtained in experiments on dogs. Thanks to slow absorption and rapid excretion, dogs tolerated well chronic fluoride poisoning. The lethal dose is between 0.7 and 4.5 g. This wide variation is due to loss by vomiting. In acute poisoning, the symptoms are nausea, vomiting, colic, and purging; salivation and lacrimation; dyspnoea and cardiac failure, tremors and convulsions; cramps, aphonia, and inability to open the mouth, albuminuria and oedema; and in the last stage, coma and respiratory paralysis. Poisoning may result from ingestion or inhalation. Hydrofluoric acid on the skin produces severe slowly-healing blisters. Necropsy shows a haemorrhagic gastritis and nephrosis. The treatment for acute poisoning is stomach lavage, lime water, milk, or a suspension of medicinal charcoal. Castor oil and large quantities of fluid should also be given. For the blistering 5 per cent soda-lime solution is also valuable.

Gettler, A. O., and Ellerbrook, L. (1939) *Amer. J. med. Sci.*, **197**, 625.

Kellner, H. (1939) *Arch. exp. Path. Pharmac.*, **192**, 549.

Lead Tetraethylbenzene ('Ethyl')

E. Storring drew attention to poisoning by lead tetraethylbenzene, 'ethyl', which is added to the fuel of motor vehicles to prevent pinking. Epileptic fits, temporary loss of consciousness, and early signs of encephalopathia saturnina were observed, but the typical signs of lead poisoning were often absent, so that the diagnosis was difficult. Poisoning by the products of combustion of lead tetraethylbenzene also presented the signs of encephalopathia saturnina, but bore more resemblance to ordinary lead-poisoning cases, as it caused colic and neuritis. Only in one case was a typical line observed on the gums. The other 4 cases had been previously diagnosed as 'idiopathic epilepsy', 'suspected malingering', and 'psychopathic constitution'. All persons coming in contact with lead tetraethylbenzene and affected by vague symptoms, especially if suggesting neurasthenia, should be examined for lead poisoning; they should generally be removed to other occupations to prevent further damage to their health.

Storring, E. (1939) *Dtsch. Z. Nervenheilk.*, **148**, 262.

— (1939) *Med. Klm.*, **35**, 801.

Chlorinated Hydrocarbons

Carbon Tetrachloride

Nephrosis.—H. Smetana reported 3 cases (2 fatal) of nephrosis due to poisoning by carbon tetrachloride, with full details of the morbid changes, and reviewed the toxic effects from an analysis of 141 collected cases. The number of cases was steadily increasing and they were due either to inhalation of fumes in a badly ventilated room when the carbon tetrachloride was in use for cleaning or in fire extinguishers, or to ingestion of the chemical. Alcoholism played a predisposing part, but its influence could not be statistically estimated, as many of the reports omitted any reference to this point. The co-worker of one of the 3 patients, a total abstainer, suffered from headache and gastro-intestinal distress after exposure in the same room to fumes, but rapidly recovered in the fresh air, whereas the patient died. The clinical picture and morbid manifestations were most characteristic, namely, headache, dizziness, general malaise, fever, sometimes irritation of the nasal and conjunctival mucosae, then nausea, vomiting, diarrhoea, and jaundice progressively deepening after some days, while the gastro-intestinal symptoms remained stationary, evidence of renal involvement became prominent—oliguria, even anuria, convulsions, acute hypertension, generalized oedema, albuminuria, nitrogen retention, and not uncommonly uraemia, and a haemorrhagic tendency. Most of the reported cases were not fatal.

Treatment included the administration of calcium carbonate or lactate, dextrose intravenously, and infusion of saline or Ringer's solution. If the chemical was swallowed, alcohol and fatty food should be avoided. The liver showed central necrosis, the kidneys were swollen and softened, the epithelial cells lining Bowman's capsule were swollen, and the space around the glomerular tuft was occupied by an albuminous cast, there were casts and necrotic changes in the cells of the renal tubules.

Ethylene Dichloride

Ethylene dichloride, or dichlorethane ($\text{CH}_2\text{ClCH}_2\text{Cl}$), is used in industry as a solvent for oils, waxes, resin, gums, and rubber, in insecticides, fumigating agents, and household cleaning solvents. Z. T. Wirtschafter and E. D. Schwartz reported 3 cases of ethylene dichloride poisoning occurring in a knitting factory, which were due to exposure when cleaning yarn. Four hours after exposure the men became dizzy, nauseated, and vomited profusely. They complained of weakness and trembling and were removed to hospital one hour later. Epigastric cramps were complained of, and in one case the liver was enlarged and tender. Leucocytosis was present in all cases and liver damage was shown by very low blood-sugar levels. All 3 patients showed a severe dermatitis of the hands which presented a raw scalded appearance. In spite of 3 weeks' treatment with bland ointments they showed a shiny thin-skinned appearance. The dermatitis was thought to be due to the defatting action and irritating effect of the ethylene dichloride. There was no evidence of kidney damage. On admission to hospital the patients were treated with injections of 10 per cent calcium gluconate. The injection produced immediate relief of the epigastric cramp, and the vomiting subsided. The next day a high calcium and high carbohydrate diet was instituted. All the patients recovered and were discharged from hospital after one week's treatment. When discharged they were advised to maintain the high carbohydrate intake.

Smetana, H. (1939) *Arch. intern. Med.*, **63**, 760

Wirtschafter, Z. T., and Schwartz, E. D. (1939) *J. industr. Hyg.*, **21**, 126.

Cosmetic Dermatitis

L. Tulipan reviews the ingredients most commonly used in cosmetics—perfume, hair dyes, cleansers, and tonics; depilatories and deodorants; face powders, creams, bleaches, and tonics, rouge, lipstick, and nail preparations; with special regard to their effect on the skin surface, and the production of a subsequent dermatitis. Cosmetic dermatitis is characterized by erythema, with oedema, and the presence of papules and vesicles with exudate, by crust formation and, finally, by desquamation. Clinically and microscopically the condition is indistinguishable from eczema. Workers in industries which produce cosmetics are frequently affected, as well as hairdressers and beauty-parlour assistants. Sensitization may be acquired immediately or through prolonged contact. Alternatively, immunity may sometimes be

acquired through long-continued exposure to the substance. A list of harmful ingredients frequently found in cosmetics includes lead in the form of lead acetate usually present in hair dyes, mercury in face creams and bleaching powder, pyridine, denatured alcohol, isopropyl alcohol, arsenic, paraphenylenediamine used in the dyeing of hair and furs, potassium carbonate, pyrogallol, alkaline sulphides, thallium acetate (a virulent poison), salicylic acid, phenol, copper, ammonium carbonate, sodium carbonate, silver nitrate, aluminium salts, quinine, quinone bodies, acetone combined with collodion to make liquid nail polish, bakelite, colocynth, dimethyl sulphate, nitrobenzene, oil of bergamot and other essential oils, synthetic oils, and alum.

Tulipan, L. (1938) *Arch. Derm. Syph., N.Y.*, **38**, 906.

TRACHEA DISEASES

See also Vol. XII, p 200.

Tuberculosis

Treatment

Electrocautery.—In tuberculous tracheo-bronchitis the lesion spreads by continuity along the submucosa and, unless it can be checked, may lead to a fatal result. F. W. Davison checked the lesion by treating the ulcer with the electrocautery through a bronchoscope. Only 1 mm. of coagulation was attempted as the object of the treatment was to stimulate the natural reparative processes and hasten cicatrization without destroying all the tuberculous tissue present. Eight cases were so treated over a period of 20 months. Treatments were given at intervals of 2 to 4 weeks. At the time of writing 6 of the patients were cured; one was improving under this treatment, and in the other the treatment had to be discontinued owing to the patient's poor general condition.

Davison, F. W. (1938) *Ann. Otol., etc., St. Louis*, **47**, 826.

Obstruction

By a Leech

O. Melikian reported on a case in which a patient complained of sudden acute and most severe symptoms of asphyxia. Laryngoscopy revealed a greenish-black undulating swelling in the region of the aryepiglottic fold, pressing against the epiglottis and obstructing the entrance to the trachea. The 'swelling' was removed and it was found to be a leech, 5 inches long and 1 inch in diameter. The author summarized the scanty literature on this subject, and concluded that the swallowing of leeches was mainly confined to the Balkan states and to Asia and occurred mostly among Mohammedans, who drank water from earthenware jugs and therefore did not see whether the water was clear or not.

Melikian, O. (1939) *Munch. med. Wschr.*, **86**, 742.

Tumours

R. J. Cann recorded 2 cases of primary carcinoma of the trachea, one squamous-celled and the other basal-celled, in women aged 56 and 71, accompanied by stridor and slight haemoptysis. One was treated by deep X-rays, the other by telurium, and in both the tumour disappeared.

Cann, R. J. (1938) *Guv's Hosp. Rep.*, **88**, 392.

TRACHOMA

See also Vol. XII, p 209, and Cumulative Supplement, Key No. 1545.

Epidemiology

Many bacteria have been found in trachomatous conjunctivitis but it is now agreed that they play no part in the aetiology. P. Thygeson and P. Richards found that the agent of trachoma, together with the viruses of inclusion blennorrhoea and psittacosis, appears to form a transitional group between the rickettsial and the typical viruses. They found that it has the characteristics of a virus in that it is

filtrable under certain conditions, forms inclusion bodies, and cannot be cultivated on non-living media

A. E. Braley studied the rickettsia bodies in trachoma. He stained with Giemsa's stain epithelial cells from normal conjunctivae, from non-trachomatous infected conjunctivae, and from trachomatous conjunctivae. He found that the inclusion bodies produced by psittacosis, a condition caused by a similar virus, were similar to the inclusion bodies of trachoma. He found mitochondria and keratin granules, stained with Giemsa's stain, in the normal epithelium and from observations on the trachomatous conjunctiva concluded that they were the bodies described and photographed by many observers in cases of trachoma rather than rickettsia bodies.

L. A. Julianelle investigated the antigenic powers of the virus of trachoma and found them ineffective. No antibodies were found in the serum of infected or recovered monkeys, the serum of patients suffering from trachoma, or in the serum of animals receiving repeated small injections of the virus from active trachomatous tissue. Monkeys which had recovered from an attack of trachoma were found to have no increased resistance to the disease.

Braley, A. E. (1939) *Arch Ophthalmol*, N.Y., **21**, 735.

Julianelle, L. A. (1939) *Amer J Pathol*, **15**, 279.

Thygeson, P., and Richards, P. (1938) *Arch Ophthalmol*, N.Y., **20**, 569.

Treatment

Sulphonamide Drugs

R. Kirk *et al* obtained encouraging results in 25 cases of trachoma by the oral administration of prontisol album. One tablet (7½ gr.) three times a day was administered in 7-day courses separated by an interval of 7 days. The corneal complications, keratitis and pannus, cleared up rapidly. This treatment is simpler and much less painful than present methods of treatment, its permanent efficacy, however, has still to be proved.

P. Richards *et al* treated 12 children suffering from trachoma with ½ gr. (0.0216 g.) of sulphanilamide per pound of body weight and an equal amount of sodium bicarbonate, given in 4 doses per day. The condition of the cornea improved during the first week of treatment. Pannus tended to disappear, and the epithelium and vessels became more normal. The conjunctiva began to improve at the end of the second week of treatment, but the follicles did not disappear until after several months. Two controls not receiving sulphanilamide showed no improvement in the trachoma until they were put on the drug, when improvement appeared in a few weeks. Whilst under treatment inclusion bodies disappeared from the conjunctiva, and it became impossible to infect baboons with the virus from epithelial scrapings. In one of the treated cases corneal infiltration persisted in spite of sulphanilamide therapy.

M. Hirschfelder described the use of sulphanilamide in 25 patients with active trachoma. Each was given ½ gr. a day per pound body weight for one week and then similarly ¼ gr. Attention was paid to possible toxic effects. While the drug did not improve cases of follicular catarrh, it diminished the epiphora of second stage trachoma. It aided milder cases in the third stage, but had little effect on the active and malignant forms characteristic of stage 4.

Hirschfelder, M. (1939) *Amer J Ophthalmol*, **22**, 299.

Kirk, R., McKelvie, A. R., and Hussein, H. A. (1938) *Lancet*, **2**, 994.

Richards, P., Forster, W. S., and Thygeson, P. (1939) *Arch. Ophthalmol*, N.Y., **21**, 577.

TRENCH FEVER

See also Vol. XII, p. 236.

H. Werner described some recent advances in trench fever (five-day fever) which after the end of the war in 1918 seemed to disappear, with the exception of an epidemic in 1934 in Poland where, in a bacteriological laboratory, 18 persons became infected. The research workers in the laboratory cultivated lice for experiments on epidemic typhus. *Rickettsia quintana* was found in the lice. These rickettsiae, which had lost their pathogenicity after many passages, seemed to have regained it. Japanese workers reported that trench fever was epidemic in Japan. N. Ogata

cultivated the virus in the testes of rabbits, and reported favourably on the treatment of neurosyphilis by this infection.

Werner, H. (1939) *Dtsch. med. Wschr.*, **65**, 174.

TRICHINIASIS

See also Vol XII, p. 241, and Cumulative Supplement, Key No 1549

Incidence

Routine post-mortem examination of the diaphragm has shown a high incidence of trichiniasis in some parts of the United States, such as Boston and New York. C. H. Evans, Jr., in 100 consecutive necropsies in Cleveland, found an incidence of 36 per cent. Examination of the diaphragm by the digestion-Baermann method alone revealed an incidence of only 20 per cent, and a combination of the compression-microscopic and the digestion-Baermann methods gave a more accurate estimate. Examination of skeletal muscles, such as the intercostals and sternocleidomastoids, give a higher incidence of infestation than examination of the diaphragm alone.

Evans, C. H., Jr. (1938) *J. infect. Dis.*, **63**, 337.

Diagnosis

Infestation with *Trichinella spiralis* is common in the United States, about 20 per cent of the population suffering from it at some time. F. B. Queen, believing that more cases would be found if aids to diagnosis were more reliable, discusses the 5 main methods of laboratory diagnosis: the differential white-cell count to detect eosinophilia, the intradermal test, muscle biopsy with histological study, the press preparation study of muscle biopsies, and the examination of muscle biopsies by the digestion method. The last 3 methods may also be applied to suspected meat. The presence of eosinophilia combined with other signs of trichinosis is very suggestive, but alone cannot be regarded as a reliable diagnostic sign, as it occurs in so many other conditions. The intradermal test is successful in diagnosis in about 90 per cent of cases. Muscle biopsy may be successful if the section happens to pass through some trichinae, but serial sections involving a great deal of work are necessary to be sure of this. The press method is difficult, and in few hands successful, but may be useful for a quick preliminary observation. In the last method the dead muscle is separated from the living trichina larvae by digestion of the muscle with artificial gastric juice. The digestate is then examined for larvae. Queen found this test 4 times more accurate than the press method. The number of trichinae per gram of muscle necessary to produce symptoms is not yet known, but in patients dying of the disease, the trichinae are usually numerous.

Queen, F. B. (1939) *Amer. J. clin. Path.*, **9**, 209.

Complications

C. H. Beecher and E. L. Amidon reported on the cardiographic condition of 44 young adults, between the ages of 17 and 20 years, who had been passed as physically fit and free from any cardiac abnormality shortly before being taken sufficiently ill with proved trichiniasis to be admitted to hospital. Out of 180 members of a Civilian Conservation Corps camp exposed to possible infection by trichinella larvae in pork, 64 gave positive skin and precipitin reactions. Two patients showed evidence of myocardial involvement, one, found clinically to have coupled beats, was proved to have nodal premature contractions which occasionally alternated with normal beats. The second patient showed prolongation of the P-R interval. In none was there any change in the T wave such as those reported by Spink. The incidence of cardiac lesions demonstrated clinically and cardiographically by Beecher and Amidon was 4.5 per cent, the damage being apparently temporary only. The details of this epidemic are promised in a paper by T. L. Feienbauch of the Department of Medicine, University of Vermont Medical College.

Beecher, C. H., and Amidon, E. L. (1938) *Amer. Heart J.*, **16**, 219.

Spink, W. W. (1935) *Arch. intern. Med.*, **56**, 238.

Treatment

In an assessment of the clinical worth of the many remedies used in trichiniasis, V. D. Van Someren found the following 3 procedures useful: (i) The oral administration of butolan—a non-toxic commercial preparation of the carbamic acid ester of *p*-oxydiphenylmethane. This is more effective than thymol preparations, but should not be used in cases of severe renal damage. Alternatively subcutaneous injections of suspensions of carvasept, a preparation of thymol in olive oil or gum acaacia, are lethal to adult trichinae, but, as one adult female may produce 200 larvae, this action may be only palliative. (ii) Three cases were treated with 3 to 7 intravenous injections of 5 c cm. of gluco-calcium. The injections were given at the height of the febrile attacks, and caused a complete resolution of the pyrexia and a vast improvement in the intestinal condition. (iii) To curtail the encystment stage, about the fourth week of the disease, injections of calcium gluconate were supplemented by vitamin D in the form of viosterol and halibut-liver oil.

Van Someren, V. D. (1939) *Brit. med. J.*, **1**, 376

TROPICAL DISEASES, GENERAL SURVEY

See also Vol. XII, p. 247, and p. 142 of this volume

About Mouk-mouk

Boalns *et al.* have reported their investigations on an epidemic eruptive disease in Central Africa, especially the Cameroons, which, though clinically presenting some resemblance to smallpox, varioloid, and chicken-pox, was sharply differentiated from them clinically, by animal inoculation, and in man by its relations to Jennerian vaccination. This disease, known locally as about mouk-mouk, was therefore a nosological entity. The authors had previously suggested that the disease might possibly be alastrim (variola minor), but, from clinical and other investigations, they have now decided against any such relationship. Four-fifths of 125 patients with about mouk-mouk showed evidence of Jennerian vaccination, usually 2 or 3 years before, which certainly did not protect against, and in fact might dispose to, the onset of about mouk-mouk. Patients during or after an attack of about mouk-mouk reacted in a proportion of about half to Jennerian vaccination. A table was given showing the points of differential diagnosis from smallpox and chicken-pox.

Boalns, Malbrant, and Dolior (1937) *Ann. Med. Pharm. colon.*, **4**

— (1939) *Bull. Acad. Méd. Paris*, **121**, 847

TRYPANOSOMIASIS

See also Vol. XII, p. 263.

Treatment

Prophylaxis

Germanin.—I. Hawking described experiments conducted in vitro on the trypanocidal action of germanin (Bayer 205) and compared its action with that of trivalent arsenicals and acriflavine. It was found that germanin had almost no trypanocidal action on *T. rhodesiense* in vitro, but that if normal trypanosomes were incubated with germanin in vitro, during which time they presumably absorb small quantities of the compound, and then washed, they failed to infect mice when injected. Trypanosomes which had been rendered germanin-resistant remained infective under these conditions. These results were in agreement with the explanation of Reiner and Kovesky that germanin had an opsonin-like effect sensitizing the trypanosomes to phagocytosis by the reticulo-endothelial system. Both normal and germanin-resistant trypanosomes exposed to germanin absorbed very little of the compound, but dead trypanosomes absorbed it more readily. By comparison, the trivalent arsenicals and acriflavine had a powerful trypanocidal action in vitro and the compounds were absorbed in very large amounts.

Curative

Undecane-1.11-diamidine.—The discovery that synthalin had a direct powerful trypanocidal action led H. King *et al.* to investigate the trypanocidal activity of

some guanidines, isothiourreas, amidines, and amines, with alkyl and alkylene chains. The most active of these drugs was *n*-undecane-1:11-diamidine, which produced permanent cure in approximately 100 per cent of mice and rabbits infected with *T. rhodesiense*. Undecane diamidine had little curative action on mice infected with *T. congolense* but, when given in large doses on the day of inoculation and the following 9 days, was useful in prophylaxis. It had no action on *T. cruzi*, *Spirochaeta recurrentis*, or *Spirillum minus* infections in mice. It acted on human simple tertian malaria, causing the parasites to disappear from the peripheral blood and the febrile paroxysms to cease. A number of aromatic amidine and guanidine compounds were prepared and showed a strong trypanocidal action in vitro.

J. Devine investigated the changes in the renal and hepatic functions produced in rabbits and in man by undecane-1:11-diamidine. In rabbits, small repeated intravenous doses were well tolerated, but a single dose equal to about half the minimal lethal dose produced a rapid rise of blood-urea of about 30 mg. per cent. There was not any change in the blood-sugar and albuminuria did not follow. The maximal tolerated dose (10 mg. per kilo body-weight) produced a transient hyperglycaemia with nitrogen retention, and lethal doses produced fatal hypoglycaemia with or without an initial hyperglycaemia. This toxic action was similar to that of synthalin. The daily oral administration of 150 mg. for 3 consecutive days in patients with induced malaria resulted in nitrogen retention but without change in the blood-sugar level. This dose caused nausea and was considered the maximal dose that could be given to such patients with safety.

Devine, J. (1938) *Ann trop Med Parasit*, **32**, 163.

Hawking, F. (1939) *Ann trop Med Parasit*, **33**, 13.

King, H., Lounie, E. M., and Yorke, W. (1938) *Ann trop Med Parasit*, **32**, 177.

Reiner, L., and Koveskatz, J. (1927) *Dtsch med Wschr*, **53**, 1988.

TUBERCULOSIS

See also Vol. XII, p. 286, and p. 39 of this volume.

Aetiology and Bacteriology

Human Form of Infantile Tuberculosis in Paris

P. F. Armand-Delille as a result of 5 years' systematic investigation and bacteriological identification of the form of the tubercle bacillus responsible for the various tuberculous lesions—glandular, meningeal, and pulmonary—found that, in Paris, tuberculosis in early life was invariably of the human and not the bovine type. By exhaustive laboratory technique this was proved in 50 cases, and further by medico-social inquiries the existence of infection in the home was established. These conclusions agreed with those of Lesne and Saenz who found that, in 176 cases of tuberculous meningitis, the human bacillus was responsible in all except 9 children who had been brought up in the country and had been fed on raw milk; in 7 of the 9 exceptions there was not any other evidence of a tuberculous environment.

Vitamin A Deficiency in Tuberculous Patients

H. R. Getz *et al.* used the biophotometer to ascertain the presence of vitamin A deficiency in 500 non-tuberculous persons and in 197 ambulant tuberculous patients. Of the group of 500, 300 were used as controls for the tuberculous group and were divided into 2 groups, one of 229 medical students (mostly male), the other of 71 junior women students. The other 200 were not used as controls as they had a suspected deficiency. The group considered to be normal in respect of vitamin A had a minimum light threshold less than 0.6 millifootcandle and low subsequent readings, while the class considered to be pathologically deficient had a minimal light threshold after the bright light above 1 millifootcandle and subsequent readings were correspondingly higher. A border-line class gave readings between these extremes. In the tuberculous group vitamin A deficiency was established in 53 per cent. In the 2 control groups the medical students showed deficiency in 6.55 per cent and the junior women students in 11.27 per cent. It was stressed that the tuberculous group consisted of mild ambulant cases, without fever and with minimal disease. It was apparent that the more advanced the disease the greater was the deficiency, but whether the advance of tuberculosis depends upon the deficiency or

the deficiency results from the infection is as yet unknown. The authors concluded that the quantities of vitamin A required varied individually, and it was not possible to state an optimal amount for adults. Apparently healthy subjects in this series showed a definite deficiency. Large doses up to 200,000 units daily were necessary to obtain normal levels in deficiency and border-line cases in this study.

Armand-Delille, P. F. (1939) *Bull. Acad. Méd. Paris*, **121**, 759

Getz, H. R., Hildebrand, G. B., and Finn, M. (1939) *J. Amer. med. Ass.*, **112**, 1308.

Immunity

H. J. Corper and M. L. Cohn found that specific immunity against infections with virulent human tubercle bacilli could not be produced by Seitz filtrates from cultures of virulent human tubercle bacilli, by highly concentrated (ultradialysis) filtrates, or by the precipitated tuberculoprotein or alum-treated filtrates. The highly concentrated filtrates, or precipitated tuberculoprotein, possess no appreciable primary toxicity for normal animals. A primary intravenous injection of large amounts of normal Seitz filtrates, highly concentrated (by ultradialysis) filtrates, or precipitated tuberculoprotein from these filtrates does not sensitize to a second intracutaneous injection with a fairly large test dose (0.1 mg.) of either filtrate or tuberculoprotein. A reaction to tuberculin can, however, be obtained in a tuberculous guinea-pig with as little as 0.000005 mg. of the same material. A primary intravenous injection of about 2 mg. of tuberculoprotein in any of the foregoing forms sensitized guinea-pigs to a lethal intravenous provocative dose (anaphylactically) of as little as 1 mg. of the tuberculoprotein in these forms. To produce cutaneous hypersensitivity to tuberculoprotein requires a small amount of avirulent human tubercle bacilli, a large amount of heat-killed tubercle bacilli (around 100 mg.), and very small amounts of virulent tubercle bacilli. There is a striking quantitative difference between the specific immune and the concomitant allergic or anaphylactic features of tuberculosis, the first being protective and the second showing a peculiar type of still unsolved intoxication.

Corper, H. J., and Cohn, M. L. (1939) *J. Amer. med. Ass.*, **112**, 403

Diagnostic Tests

According to H. Behrendt much harm can be done by indiscriminate tuberculin tests, and the following course should be adopted in the use of tuberculin reactions: On normal children—(a) cutaneous (Pirquet) test with undiluted tuberculin, or percutaneous test with diluted tuberculin ointment, or intracutaneous injection of 0.0001 mg. of tuberculin. If this test is negative (b) either repetition of the above procedure or further intracutaneous test with increasing doses from 0.0001 mg. to 0.01 mg. On children who are likely to be hypersensitive (a) cutaneous (Pirquet) test with 1 in 10 tuberculin, if no reaction, to be followed by (b) cutaneous test with undiluted tuberculin, by percutaneous test with diluted tuberculin ointment, and finally by intracutaneous injections of 0.01 mg. tuberculin. No tuberculin test should be made on children who are known to be tuberculin-positive.

The Tuberculin Patch Test

Because of the intense local reaction and fever sometimes caused by the Mantoux test, H. Vollmer and F. W. Goldberger increased the potency of the tuberculin patch test to make it approximate to the Mantoux test (0.1 mg.) and compared the results obtained from both tests in 169 children known to be tuberculous. Of these only one, who had reacted to the Mantoux test with the stronger solution of purified protein derivative, failed to react positively to the tuberculin patch test. In 118 children suffering from various diseases, who were investigated after admission to hospital, the Mantoux test, even when 1 mg. of old tuberculin was used, did not reveal a single case of tuberculous infection which had not already been discovered by the tuberculin patch test.

A comparative study of the tuberculin 'patch' test (Vollmer, Lederle) and the intracutaneous Mantoux test was carried out in children at the Great Ormond Street Children's Hospital by D. Court. Two groups of children were tested by both these methods. In the first group of 110 cases taken in a routine fashion without any regard to age, sex, or clinical diagnosis there was not any difference in the results obtained from the 2 methods. In the second 100 cases on whom a positive Mantoux test had already been established the results were: Mantoux-positive, 100;

patch-positive, 98; patch-negative, 2. The patch test in general is slightly less reliable than the Mantoux, but was positive in 95 to 98 per cent of cases. The balance (2 to 5 per cent) required additional investigation which was best furnished by a Mantoux test using a 1 to 100 dilution. The advantages and disadvantages of the patch test were described. The advantages were: simplicity in technique; the fact that the material can be preserved in a cool dry place for a year; and the absence of complications. The disadvantages were the slightly less reliability and the occasional occurrence of local skin reactions. If doubt still remains, the result of the intradermal test should be accepted as final.

W. D. Steward also discussed the advantages of the tuberculin patch test over the Mantoux method. A series of 91 tuberculous institution children and 5 normal adults were investigated. Half the patch tests were prepared from old beef extract medium and half from a synthetic medium (Seibert's formula). Little difference was noted between the two types of patch test. The test is particularly useful in children because it is painless.

The Mantoux Test

According to D. B. Bradshaw, Immunological Officer at the Hospital for Sick Children, Great Ormond Street, the value of the Mantoux test is considerably greater than usually recognized. In 3,010 children tested between 1934 and the middle of 1938 there were found 748 positives (25 per cent). The tests were performed with 0.1 c.cm. or 0.15 c.cm. of 1 in 1,000 tuberculin and the skin was examined between the third and the seventh day. Doubtful cases were retested with a 1 in 100 dilution of tuberculin. The Mantoux test excluded a diagnosis of tuberculosis in 3 out of 4 'suspects' up to the age of 8, and in more than half of the suspects from 10 to 12.

Single Injection Mantoux Test

D. Anderson and C. Harvey suggest the use of a single injection technique for the Mantoux test, in place of the usually accepted 2 injections. In this latter case the first injection consists of 0.00002 mg. of tuberculin P.P.D., followed by a second of 0.005 mg. when a reaction has not occurred after the first. In the single injection method, the dose is 0.00125 mg. in 0.025 c.cm. of diluent. Sharp reactions are comparatively frequent, but a much smaller cutaneous area is affected. It is not so inconvenient for the patient, and the results are considered equal to the 2-injection method.

Tuberculin Ointment Test

The Mantoux intradermal test for tuberculosis, which is most reliable, has the disadvantages that it must be performed by someone with knowledge of the technique and that the injection is troublesome especially in children. H. P. Wright *et al.* adopted Hamburger's percutaneous ointment for tuberculin testing, which could be rubbed into the skin by general practitioners or nurses. The ointment consisted of 1 c.cm. of old tuberculin, 1 g. of fuller's earth, and 7.8 g. of lanolin. A small piece the size of half a dry pea was rubbed into an area over the sternum the size of a florin with 60 revolutions of the finger. The test was carried out in 44 children (aged 23 months to 13 years) known to have tuberculosis and positive Mantoux reactions. Within 12 hours 73 per cent of the tuberculous cases showed pale or pinkish papules, either alone or with surrounding zones of erythema and skin induration; after 24 hours this reaction was present in 94 per cent, and after 48 hours 100 per cent of the cases. The reaction persisted for a week in 79 per cent of cases. Fifty-seven patients in the general medical wards, where all patients were given a Mantoux test as a routine, were tested with the ointment; 3 of them gave a positive result, the same 3 patients who had a positive Mantoux reaction.

Teeth as Indicators of Tuberculosis

G. F. King-Turner suggested that the teeth may act in the majority of cases as indicators of past or active tuberculosis. His experience led him to assume that the findings were in the main significantly constant. The balance of the blood reaction is of primary importance to the dental tissues. An acid reaction, as measured in the saliva, leads to the withdrawal of calcium ions from the enamel of the teeth, so that the dentine finally becomes exposed and caries sets in. In many cases this appearance of dental caries coincides with activity of the tuberculous lesion. If a patient with a tendency towards acidosis develops tuberculosis, it is unlikely that he will have sufficient ionized calcium to calcify the lung conditions.

Already the calcium reserves will have been depleted in an attempt to compensate for the acid tendency. In pyorrhoea, which may be said to be biochemically antagonistic to the caries found with acidosis, the reverse has occurred. Increased alkalinity had caused the calcium ions to be built into the enamel of the teeth, resulting in the latter becoming denser in consistency. An abundance of base remains in the blood, which is easily precipitated. The author argues against wholesale removal of the teeth on the grounds of their importance as diagnostic factors.

Guinea-Pig Inoculation

F. L. Pickof devised a method of guinea-pig inoculation for the diagnosis of tuberculosis which gave information in about one-third of the time usually required for diagnosis. If the guinea-pig were first subcutaneously injected with 1 to 1.5 c.cm. of a suspension of fine amorphous silicon dioxide and then injected through the same puncture with the suspected material, an infiltrated area developed at the site of injection in 10 to 12 days. Material removed from this area with a syringe and stained by the Ziehl-Neelsen method showed the presence of tubercle bacilli in a positive case and in a series of laboratory experiments in which known tuberculous material was used. In a control group the test was always negative. If it is not positive on the tenth or twelfth day, another examination should be made 2 or 3 days later. The guinea-pig should always be kept alive for 4 more weeks so that the earlier findings may be checked by autopsy.

Anderson, D., and Harvey, C. (1938) *Med. J. Aust.*, **88**, 378

Behrendt, H. (1938) *Acta paediatr., Stockh.*, **23**, 129

Bradshaw, D. B. (1939) *Brit. med. J.*, **1**, 825

Court, D. (1939) *Brit. med. J.*, **1**, 824

King-Turner, G. I. (1939) *Tubercle, Lond.*, **20**, 311

Pickof, F. L. (1939) *Amer. J. clin. Path.*, **9**, 339

Steward, W. D. (1938) *J. Pediatr.*, **13**, 510

Vollmer, H., and Goldberger, F. W. (1938) *Amer. J. Dis. Child.*, **56**, 584

Wright, H. P., Chaisson, A. F., and Allison, R. (1938) *Canad. med. Ass. J.*, **39**, 123

Prevention

W. Ogden, with nine collaborators, outlines a method of tuberculosis control which has been practised at the Toronto Western Hospital Chest Clinic for 15 years. It consists in a preliminary intracutaneous or Mantoux tuberculin test which, if negative, is repeated. All patients giving positive results are subjected to serological tests (the tuberculo-complement-fixation and the Caultield inhibitive reaction). When positive results are obtained, advice is given regarding mode of living, diet, and rest. These factors are regulated by the results of repeated serological tests. The author states that over a period of 15 years a total of 1,300 known contacts and 400 normals have been under observation and of those who have followed the prescribed regime, not one has developed tuberculosis. By means of these tests contacts may be diagnosed and preventive treatment instituted months before diagnosis by physical signs and symptoms or by X-ray is possible. The suggestion is made that the entire population could be controlled in this way, commencing with semi-annual tuberculin skin tests.

Prophylactic Immunization

Multiple puncture vaccination—S. R. Rosenthal advocated the multiple-puncture method of BCG vaccination, and this procedure has attracted investigation in Paris. L. Nègre and J. Bretey of the Pasteur Institute, from experiments on guinea-pigs involving 30 and 50 punctures in two series, concluded that the method of multiple punctures was as efficacious as the vaccination subcutaneously or intradermally usually employed, in its prophylactic and sensitizing effects. Multiple scarification was as satisfactory as multiple punctures. B. Weill-Hallé, Director of the School of Child Welfare of the Faculty of Medicine, pointed out that, during the 18 years' employment of Calmette and Guérin's BCG, various forms of technique have been tried—oral, subcutaneous, intramuscular, intradermal; and that, without doubting the value of the others, preference had been given to the subcutaneous for its simplicity and efficacy in producing allergic sensitivity in 6 to 8 weeks, by a dose of $\frac{1}{10}$ mg. A trial has been made in infants

of Rosenthal's method, with slight modifications, especially the substitution of scarifications for punctures. So far the results had been satisfactory, and certainly free from any untoward effects in the scarified area; but more prolonged observation was obviously necessary with regard to the protective and immunizing effects.

Nègre, L., and Bretey, J. (1939) *Bull. Acad. Méd. Paris*, **121**, 836.

Ogden, W. (1939) *Canad. med. Ass. J.*, **40**, 253.

Rosenthal, S. R. (1939) *Amer. Rev. Tuberc.*, **39**, 128.

Weill-Hallé, B. (1939) *Bull. Acad. Méd. Paris*, **121**, 890.

Treatment

Antituberculosis Endotoxoid

Antituberculosis endotoxoid alone and in combination with specific serum was used by F. Grasset in the treatment of 242 cases, of these 230 were pleuropulmonary; 5 were laryngeal, 5 were urogenital, 4 peritoneal or intestinal, 3 glandular, 7 ocular; and 7 were bone tuberculosis cases. The endotoxoid consisted of the antigenic principles liberated by smooth strains of the tubercle bacillus, heated to a certain temperature and then submitted to a freezing process. The antigen contains the water-soluble specific lipid of the tubercle bacillus and a small proportion of bacillary protein, and by submitting the preparation to formalin after the addition of hydrolysed peptic medium, an atoxic stable vaccine results, which can be injected causing little or no reaction. Dosage was commenced with 0.05 c.c.m. given twice a week, this was doubled in the second week and then increased by 0.1 c.c.m. until 0.5 c.c.m. bi-weekly was reached. Doses of 1 c.c.m. may then be given at weekly intervals and may continue over a period of months. Good therapeutic results were obtained after a few weeks, general improvement being noted, coupled with increased function of the affected organs. Definite regression of infection occurred, with some regeneration of the parenchymatous tissue and fibrotic cicatrization. Pyrexias were reduced. In a group of 41 cases of pulmonary tuberculosis, 32 benefited and 11 did not. There were 5 deaths amongst the latter, but all these had shown third stage lesions at the commencement of treatment, and considerable clinical improvement marked the course of the therapy. For various reasons relapses occurred. In another series of cases infection was arrested in all first stage patients and in 29 per cent of the second stage. Particular benefit was derived in the case of multiple cavities by the combined use of artificial pneumothorax and endotoxoid. In a group of patients treated with serum and endotoxoid, 39.4 per cent were definitely benefited, 29 per cent did not improve, and 31.2 per cent died. This incidence of improvement was considered very satisfactory in this group, which was composed of natives, whose susceptibility is more marked. A few Europeans were included, all of whom showed positive sputum and advanced lesions, many of them bilateral, when treatment was instituted.

Surgical Tuberculosis

Rubrophén. H. Schaer treated 41 cases of surgical tuberculosis with rubrophén. The drug is trimethoxy-dioxyotritan ($C_{22}H_{20}O_6$), it is easily soluble in water if combined with sodium bisulphite. It is only slightly toxic and is excreted almost completely through the kidneys. Rubrophén may be used either in the form of tablets, by injection, or as an ointment (5 per cent), the last should be used for skin tuberculosis. The drug is useful only in surgical, and is useless in pulmonary, tuberculosis. In 10 to 20 per cent of the patients there is, a few days after the beginning of the treatment, a focal reaction with fever and pain. This is a good sign. It is followed by increase of weight and general improvement of the condition. In about 70 per cent of the cases, cure (according to Hungarian authors) should be accomplished in half the time required for any other treatment. The author did not agree with that figure, he saw an improvement in certain types of surgical tuberculosis and thinks the treatment should be used in combination with other types of treatment.

Grasset, E. (1939) *Tubercle*, **20**, 397.

Schaer, H. (1939) *Schweiz. med. Wschr.*, **69**, 369.

TUBERCULOSIS, GENERALIZED

See also Vol. XII, p. 298.

Combined Pulmonary and Extra-Pulmonary Tuberculous Lesions

O. Marienfeld analysed 100 cases of extra-pulmonary tuberculosis and reviewed the publications on the combined occurrence of pulmonary and extra-pulmonary tuberculous lesions. Among the 100 adult patients (80 male, 20 female) 74 showed skeletal tuberculosis, and of these 74 cases, 19 presented in addition evidence of extra-pulmonary visceral involvement. The main foci in bone were in the hip, spine, and knee. In the remaining 26 cases the extra-pulmonary foci were in the urogenital tract (10), lupus (6), and lymphatic glands. In 29 of the 100 extra-pulmonary cases of tuberculosis the lungs were described as free from tuberculosis. In about 70 per cent of the 71 combined cases it was possible to state definitely which of the two lesions had appeared first. In 26 cases (group A) the extra-pulmonary lesion was the older, and in 25 cases (group B) the pulmonary lesion was the first to be recognized. The average interval between the appearance of the two lesions was 13 years in group A, and 6½ years in group B. The prognosis was bad in one-fifth of group A, and in four-fifths of group B.

W. Pagel, also from Papworth Village Settlement, has supplemented the above observations by a description of the morbid anatomy of the pulmonary lesion in extra-pulmonary tuberculosis, based on 23 necropsies of chronic extra-pulmonary tuberculosis. There is hardly any doubt that the lesions in the lungs in extra-pulmonary tuberculosis differ radiologically and on post-mortem examination from those of ordinary isolated pulmonary tuberculosis in adult life. In 15 out of 23 necropsies, made in the 5 years 1933-8, the lesions in the lungs were those characteristic of chronic disseminated tuberculosis, namely, a chronic military condition, discrete and cortico-pleural spread, haematogenous emphysematous tuberculosis, numerous calcified round infiltrations, and punched-out cavities.

Marienfeld, O. (1939) *Papworth Rev. Bull.*, **1**, 37.

Pagel, W. (1939) *Papworth Rev. Bull.*, **1**, 57.

TULARAEMIA

See also Vol. XII, p. 309.

Clinical Picture

M. Peltier *et al.* brought forward evidence, mainly retrospective, from positive agglutination reactions of a relatively high dilution for *Bacterium tularensis*, in 3 patients, that in East Africa there was a typhoid-like form of tularaemia—a disease never previously described in the tropics. The symptoms of these patients were high fever, intense headache, some degree of the typhoid state, pains in the joints, a papulo-vesicular eruption, followed by generalized desquamation, a more or less prolonged course, and slow convalescence with asthenia. Laboratory tests for the enteric and typhus fevers, and blood cultures, were negative. Although this typhoid-like form only was observed, it was thought that the glandular form of tularaemia might also exist in Senegal.

Peltier, M., Arquie, E., Jonchère, H., and Durieux, C. (1939) *Bull. Acad. Méd. Paris*, 3^e sér., **121**, 562.

Diagnosis

S. F. Friedewald and G. A. Hunt studied the laboratory tests for the diagnosis of tularaemia in 50 cases. If specific tularensis antiserum is to be used in the treatment of the disease, it must be used early, and it is therefore vitally important to have reliable methods of diagnosis. One method of diagnosing the disease is by blood agglutination, and the authors found this to be very reliable after the first week of the disease. The opsono-cytophagic reaction is of value also in the first week, and is useful in differentiating brucellosis from tularaemia when cross-agglutination occurs. Skin tests may be either antigen or antiserum tests. Of these the first was found very reliable and specific during the first week of the disease, but the second gave only a small percentage of successes. This failure is due to reactions to the control serum which it is necessary to use in this test. The culture

of the organism is the most definite method of diagnosis, but it requires so much time that it is rarely necessary to do it, especially as some of the above tests are so reliable.

Friedewald, S. F., and Hunt, G. A. (1939) *Amer. J. med. Sci.*, **197**, 493.

TUMOURS

See also Vol XII, p. 313.

Diagnosis of Malignancy

By the Mitosis Coefficient

W. B. Dublin determined 'mitosis coefficients', i.e. the number of mitotic figures per 1,000 tumour cells, in 100 squamous-cell carcinomas of the lip and skin, 100 fibrosarcomas of the extremities, 62 basal-cell carcinomas, and 10 non-melanotic melanocarcinomas. The mitosis coefficient was found to give a fair index of malignancy when compared with 5-year survivals in low-grade fibroblastic tumours; an increase in the number of mitotic figures was the earliest and most constant sign of malignancy. A rapid method of estimating the mitosis coefficient is described.

The 'Serum-Boiling' Test

H. F. Kurten describes two different forms of coagulation which occur on heating human serum. The one reaction—dissolution into protein bodies which cling to the wall of the test tube—takes place in normal serum and in the serum of patients suffering from a number of diseases. The other form—after preliminary 'foaming' the serum recedes and shrinks into a thick jelly—is characteristic of malignant tumours. This phenomenon, called by the author the serum-boiling test, also appears in a few acute or chronic conditions, but it was found that it disappeared after cure of these, whereas it persisted in persons suffering from malignant tumours. The serum is mixed with 0.8, 1.2, 3.4, and 5 parts of isotonic saline and heated; the reaction is most apparent if 1 part of serum is mixed with 0.8 parts of saline. The test was carried out on 109 established cases of carcinoma and on a large number of controls.

Dublin, W. B. (1939) *Proc. Mayo Clin.*, **14**, 364.

Kurten, H. F. (1939) *Klin. Wschr.*, **18**, 667.

Treatment

Organotherapy

G. Sakharov and D. Rossijsky published their experimental findings on the treatment of malignant tumours by a product which had as its principal constituent an aqueous extract of the adrenal cortex. They found that this product had an anti-adrenaline effect; the doses used on cancerous patients were 0.3 to 1.0 c.cm. by hypodermic injection every third day. There was a slight local reaction. The authors concluded that organotherapy can be successful in chosen cases. Gonococcal vaccine was used in addition to organotherapy in some cases, on account of its stimulating action on the reticulo-endothelial system.

Sakharov, G., and Rossijsky, D. (1931) *Acta med. U.S.S.R.*, **1**, 145.

TYPHUS FEVERS

See also Vol XII, p. 325.

Typhus Fever in South Africa

J. H. Gear of the South African Institute for Medical Research, Johannesburg, investigated the forms of typhus fever in South Africa, namely, louse-borne, rat-flea-borne, and tick-borne, and provided many statistics. No case of mite-borne typhus has yet been recorded there. Louse-borne typhus was one of the major health problems in the country. Thus in 1935 there were 6,826 cases and 996 deaths in non-Europeans, and 97 cases and 5 deaths in Europeans, and in that year in the mortality of infectious diseases typhus came second to tuberculosis. In the 5,956 cases notified in 1934 the death-rate was 11 per cent. Most outbreaks occurred in rural districts, in or near Native Reserves. In natives (Bantus) the rash was

difficult to detect, and conjunctival congestion and the 'parrot eye' appearance helped in the diagnosis. Complications were common, especially pneumonia and gangrene of the extremities, usually the legs. Tick-borne typhus, like louse-borne, had an incubation period of a week, was wide-spread, and in the more temperate high veld of South Africa had a seasonal incidence, most cases occurring in the summer months when ticks were numerous, on the low veld where the temperature was more even, cases occurred with equal frequency throughout the year. In South Africa tick typhus was a mild disease, dangerous in old age and the debilitated only. One case only of rat-flea (murine) typhus was examined in this investigation. The laboratory investigations were very fully reported.

Gear, J. H. (1938) *S. Afr. J. med. Sci.*, **3**, 134.

UNDULANT FEVER

See also Vol. XII, p. 361

Treatment

Sulphonamide Drugs

J. E. Debono, after treating 25 cases of undulant fever due to *Brucella melitensis* with 4.5 g. of prontosil daily for 7 days, is of opinion that in no case could recovery be entirely attributed to this therapy. If the drug was given during the decline of a pyrexial wave, the temperature continued to fall gradually, only to rise again in a few days in spite of the continuation of the prontosil therapy. If treatment coincided with the ascent, the temperature continued to rise. In 'septicaemic' cases, the effect appeared to be definitely harmful.

C. Z. Neumann employed intramuscular injections of prontosil red (5 c.c.) on alternate days in 4 cases of undulant fever, in only one was the period of the disease perceptibly shortened. To 16 other patients prontosil red was given orally and in 15 the average duration of the fever was 7 days, ranging from 2 to 12 days. As a rule untreated patients required 2 to 6 months to become free from fever. The treatment should be continued for a few days after the temperature had become normal. The initial dose for children was 4 tablets daily and for adults 6, after 3 or 4 days, the tablets were reduced to 3 for children, and to 4 or 5 for adults, at the end of a week children were usually given 2 tablets and adults 3 tablets daily. No severe toxic reactions were noticed, but a curious lassitude was sometimes obvious after 2 days' treatment and lasted for 2 or 3 days. In 3 cases there was slight vomiting. Loss of appetite, usually stated to be due to the drug, was very common in undulant fever and did not appear to be aggravated by prontosil.

R. H. Fraser, F. D. White, and M. B. Perrin recorded two typical cases of undulant fever, one of a barrister whose occupation led to attendance at a dairy farm, where he subsequently drank some milk, and the other of an employee at an abattoir. Treatment in both cases consisted of the administration of prontosil and sulphanilamide, the first patient having had preliminary injections of Foshay serum for one month. Both patients reacted favourably, regained appetite, and put on weight.

W. T. Bynum described 6 cases of undulant fever—2 cases of acute, one subacute, and 3 chronic—which were treated by maximal therapeutic doses of sulphanilamide. The 6 treatments were entirely unsuccessful and do not endorse the usual wide claims made for this drug.

Bynum, W. T. (1939) *J. Amer. med. Ass.*, **112**, 835.

Debono, J. E. (1939) *Brit. med. J.*, **1**, 326.

Fraser, R. H., White, F. D., and Perrin, M. B. (1938) *Canad. med. Ass. J.*, **39**, 455.

Neumann, C. Z. (1938) *Brit. med. J.*, **2**, 342.

URETHRA, DISEASES

See also Vol. XII, p. 386, and p. 156 of this volume.

Urethritis

Treatment

Sulphanilamide—G. Jose describes the routine treatment of urethritis and its complications with sulphanilamide. He finds that 2 g. daily is the average dose for

ambulatory patients, and 3 g. the maximal daily amount, given orally in divided doses. Other treatment includes the alkalinization of the urine, with low-pressure urethral irrigations and anterior urethral instillations. Prostatic massage is given twice a week to patients with posterior urethritis and prostatitis. The administration of sulphanilamide is stopped if headaches or rashes develop. When treatment is begun on the first or second day of gonococcal urethritis, excellent results are obtained in 70 to 80 per cent of cases, active therapy being continued for 3 or 4 weeks. When treatment is begun at any time between the fourth and fourteenth day, about 50 per cent respond rapidly. The administration of sulphanilamide is found to have little effect on epididymitis. The author finds that, in cases in which the drug is likely to be effective, improvement will be obtained within a few days. Uleron has been used when sulphanilamide evoked no response, the dosage being 3 g. per day. The author thinks that it is more effective once a leucocytosis has developed—from the eighteenth day onwards. Rapid results appear to be obtained, but recurrences are common.

Jose, G (1939) *Med J. Aust.*, **1**, 54.

Mycotic Urethritis

C Pisacane and A Coppolino described 5 cases of mycotic urethritis in males, 4 of whom came from Africa and one from Messina. In 3 cases cultures were obtained of *Cryptococcus ruber*, in one of *Penicillium candidum*, and in one of Castellani's *Monilia tropicalis*. The incubation period was long, the minimum being 15 to 30 days and the maximum several months. A slight urethral discharge was the only symptom, and all the patients rapidly responded to bland treatment, such as hexamine and irrigations of potassium permanganate or mercuric oxyecyanide.

Pisacane, C., and Coppolino, A. (1938) *J. trop. Med. (Hyg.)*, **41**, 332

Tumours

Melanoma—H I Sain recorded a primary melanoma of the urethra, near the glans penis in a man, aged 70, and collected 9 reported cases, 3 in men and 6 in women, which were analysed. The tumour might be flat or pedunculated, and histologically was composed of compact masses of irregular polygonal or large spindle cells with clumps of brown-pigment granules in the cells or outside them. Swelling, dysuria, lateral deviation of the urinary stream, and a foul discharge were the chief clinical manifestations. In females a blood-stained discharge might suggest disease of the genital tract.

Sain, H E (1939) *Amer. J. Cancer*, **36**, 243.

URINE EXAMINATION

See also Vol. XII, p. 393

Bacteriology

T L. Schulte studied the bacteriology of the normal urine in males and females. He found that the following organisms, in this order of frequency, appeared in the urine: *Micrococcus ureae*, diphtheroids, *Streptococcus faecalis*, alpha streptococcus, gamma streptococcus, *Staphylococcus albus*, *Escherichia coli*, *Aerobacter aerogenes*, and *Pseudomonas*. The alpha streptococcus appeared in the prostatic secretion of the male. The *Staphylococcus albus* was never found in normal urine. To test the urea-splitting power of the bacteria, Schulte used a medium consisting of sodium chloride and peptone in distilled water. Alcoholic thymol blue was used as an indicator and the pH adjusted to 7. A 10 per cent solution of urea was added and the whole incubated with the organisms at 37.5° C for 48 hours. The formation of a greenish colour showed a slight ability to split urea but the presence of a purple colour showed a true urea-splitting organism. The organisms which were true urea splitters were *Proteus ammoniae* and *Micrococcus ureae*. The pathogenicity of the organisms was measured either by injection into animals or by inoculating a small tube containing 0.5 c.m. of human or horse plasma with a pure culture of the organism and incubating it at 37.5° C. A gel forms in from 8 to 24 hours if the test is positive. This last test is only applicable to mass-forming Gram-positive cocci.

Schulte, T. L. (1939) *Proc. Mayo Clin.*, **14**, 249.

UROGENITAL ORGANS, ABNORMALITIES

See also Vol. XII, p. 401.

Ureterocele

R. Gutierrez defined a ureterocele as a cyst-like formation that arose when the vesical end of the ureter became stretched out into an abnormal dilatation as the result of narrowness of the orifice, or a congenital or acquired stenosis of the orifice led to such a dilatation of the ureter within the bladder. The outer covering of the swelling is composed of bladder mucosa. Of the 18 cases treated by the author 5 were unilateral and 10 bilateral, 2 cases had a stone in the ureterocele and one was a blind ureterocele with calcification of the corresponding functionless kidney.

The clinical symptoms differ little from cystitis and allied conditions. Intravenous urography is of great help in accurate diagnosis, and its use as a routine measure was advocated by the author.

The treatment consisted of dilations of the mouth of the ureterocele with ureteral bougies and irrigations of the renal pelvis and the ureters with antiseptics such as silver nitrate and acriflavine. Minor trans-urethral surgical measures should be employed when possible, and consist of simple fulguration of the ureteral orifice with a point electrode performed through a cystoscope, or, as an alternative, ureteral meatotomy, using the electric cutting-current and minute cystoscopic scissors, or a knife electrode. A loop electrode is sometimes used. When the condition is more advanced, the ureterocele is of large dimensions, and when the kidney function has been lost through the obstructive effect, with probably an associated hydro-ureter and hydronephrosis, radical surgical measures become necessary.

Gutierrez, R. (1939) *Surg. Gynec. Obstet.*, **68**, 611

Congenital Absence of Penis

G. J. Rukstnat and R. J. Hasterlik reported the case of a premature boy with congenital absence of the penis, anus, prostate, and urethra, with a fistulous track connecting the atretic colon with the urinary bladder. There was severe inflammation of the kidneys ascribed to the irritating effect of bile which entered the urinary tract from the meconium. From a review of the recorded cases it was concluded that there had been only 10 incontrovertible cases. In some cases so entitled, the condition was hermaphroditism, epispadias, or scrotal or perineal penis. The malformation was usually part of a larger congenital deficiency. The condition of the kidneys was that of severe chronic inflammation with advanced benign nephrosclerosis, and very different from the hydronephrosis due to obstruction to the urinary outflow.

Rukstnat, G. J., and Hasterlik, R. J. (1939) *Arch. Path.*, **27**, 984

UTERUS, DISEASES AND DISORDERS: PHYSIOLOGY

Motility of Uterus

L. Wilson and R. Kurzrok investigated the motility of the human uterus by inserting into the uterine cavity a sterile rubber balloon which was filled with 15 c. cm. of air, and attached to a sensitive recording kymograph. The pressure changes were transmitted to a column of mercury on which floated a recording pen. Records were taken for about 45 minutes; 29 patients were investigated and a total of 187 tracings taken. It was found that, during the follicular phase of the menstrual cycle, high tonus and small rapid contractions were present. In the luteal phase there were low tonus and slow contractions of great amplitude. The endometrial changes occurring before each phase of the cycle were shown by a characteristic myometrial lag. Patients with dysmenorrhoea had exactly the same tracings as those with painless periods, but those with proliferative or cystic endometrium showed only tracings of the follicular phase proving an absence of the corpus luteum hormone. Posterior pituitary extract stimulated the uterus during the whole of the cycle, but most of all during the luteal phase.

Wilson, L., and Kurzrok, R. (1938) *Endocrinology*, **23**, 79.

UTERUS DISEASES AND DISORDERS: GENERAL DIAGNOSIS

Biopsy of Uterine Mucosa

B. Lorincz and A. Davis have evolved a method by which small fragments of the uterine mucosa may be removed from the unanaesthetized patient in the out-patient department or the consulting-room. It is applicable to those conditions in which curettage is contra-indicated by the presence of pyrexia, active adnexal inflammation, or suspected ectopic gestation. The apparatus (see Fig. 26) consists of a cannula and a suction pump. The cannula is a rigid tube 8 inches long, bent at 30° at one end and at 90° at the other. The former (uterine) end is closed but is perforated by two small holes measuring approximately 0.25 cm. in diameter. The other end is open and fits into the rubber stopper of a small receiving bottle. There is also a short tube attached at right angles to the main one; this is open to the air, and its purpose is to prevent the formation of a partial vacuum. Within the main tube is a much finer tube, which admits air to the uterine end of the aspirator. The difficulty caused by the varying positions of the uterus is met by the provision of 2 aspirators bent in opposite directions at the uterine end, one for anteversion and the other for retroversion. The diameter of the outer tube is equal to that of a No. 4 Hegar dilator, so that it may easily be passed into the multiparous uterus. In nulliparae it may be necessary to dilate the cervix slightly before the instrument can be introduced. The technique is

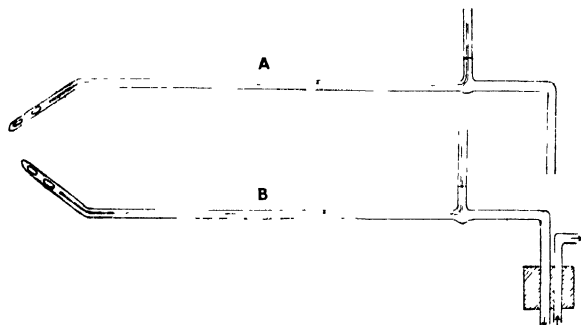


FIG. 26. Diagram of the intra-uterine aspirator. A is for use in the retroverted uterus, B when it is anteverted. The aspirator contains a long fine glass tube for the admission of air, and is perforated at the uterine end by two small oval holes. The distal end passes into a bottle, which is itself evacuated by an electric suction pump. (From *British Medical Journal*, 1939)

simple. A speculum is placed in the vagina and the cervix seized with a single volsellum. The left lateral position is usually the most satisfactory. The vaginal cervix is then carefully cleaned, and the sterilized aspirator introduced into the uterus. Gentle suction is commenced, either with a breast-pump motor or a large syringe, the aspirator being rotated continually so as to obtain tissue from several parts of the endometrium. The suction is continued until an amount of material adequate for microscopical examination is collected, when the cannula is gently withdrawn. The use of the aspirator is indicated in suspected ectopic gestation, acute endometritis, tuberculosis of the endometrium, long-continued slight post-partum haemorrhage, and in the study of various endocrine disorders and their reaction to hormone therapy. In some of these conditions ordinary curettage is dangerous, and others do not warrant a surgical operation, however minor.

Lorincz, B., and Davis, A. (1939) *Brit. med. J.*, 1, 261.

UTERUS, DISEASES AND DISORDERS: DEVELOPMENTAL ABNORMALITIES

See also Vol. XII, p. 416.

Underdeveloped Uterus

Treatment

Gonadotrophic hormone therapy.—S. A. Payne and E. K. Shelton observed the

effect of the gonad-stimulating substance in anterior pituitary extract on 10 patients with small uteri, none with a uterine depth of more than 2 inches. An underdeveloped uterus might not cause any symptoms and might function adequately, even to pregnancy. Most of these showed some abnormality of menstrual function, such as delayed onset of the period or oligomenorrhoea. Some patients were of masculine habitus and 3 were of eunuchoid type. All showed atrophy of the endometrium on biopsy at the third to fourth post-menstrual week. Eight cases showed a response to treatment; in 7 there was improvement in menstruation and the endometrium became more normal after the injections. All except one were given some thyroid in the later weeks. One patient became pregnant, which suggested that the anterior pituitary extract might have an influence on ovulation. The endometrium changed to the secretory type in 4 cases and one patient did well on thyroid alone. Uterine growth took place in 3 cases.

Payne, S. A., and Shelton, E. K. (1938) *Endocrinology*, **23**, 598.

UTERUS, DISEASES AND DISORDERS: TUBERCULOSIS

Of Endometrium

C. F. Tessmor of the Mayo Clinic reported a case of tuberculous disease of the uterine endometrium in a patient aged 68. The uterine (I allopian) tubes were not infected and the uterine disease was regarded as blood-borne rather than as a descending infection, as was generally believed. The patient also had bilateral ovarian xanthofibromas, and a simple ovarian cyst containing multiple intracystic fibromas. The incidence of uterine tuberculosis, which was rare at the Mayo Clinic, was discussed, and some statistics quoted, e.g. that it was found in about one in every 400 gynaecological laparotomies.

Tessmor, C. F. (1938) *Proc. Mayo Clin.*, **13**, 721.

UTERUS, DISEASES AND DISORDERS: TUMOURS

See also Vol. XII, p. 448.

Fibroid Tumours

Treatment

Surgical. In an investigation of 523 abdominal myomectomies performed for uterine myomas, V. S. Counseller and R. E. Bedard found that, during the same period, hysterectomy had been performed for fibromyomas in about 3,400 cases. The site of the tumour was important as they should be enucleated through the anterior surface of the uterus or through the anterior leaf of the broad ligament so as to minimize the risk of subsequent intestinal obstruction. In pregnancy myomectomy was indicated in exceptional circumstances only, of 22 pregnant women operated on 30 per cent miscarried. In this series the recurrence rate of fibromyomas after this operation was 20 per cent.

Counseller, V. S., and Bedard, R. E. (1938) *J. Amer. med. Ass.*, **111**, 675.

Carcinoma of Cervix Uteri

Aetiology

G. I. Strachan studied the changes in several hundred cervixes which were removed at operation on account of chronic inflammatory lesions. The lacerated, everted, badly eroded cervix was no more prone to carcinoma than more superficial erosions. The rare condition of visible leucoplakia of the cervix, a white stippling of an erosion, can only be seen with a magnifying colposcope. It is definitely precancerous. Histologically, hyalinization of the subepithelial stroma in old-standing cases is probably precancerous. An increase in epithelial thickness is of no significance, but pointed epithelial downgrowths, if not due to oblique sectioning, are suspicious. Irregular cytoplasmal staining, hyperchromatism, and mitosis are also important.

Morbid Anatomy

Glandular changes.—F. J. Taussig removed 1,271 lymph glands from patients with carcinoma of the cervix or vulva, taking them from the inguino-femoral chain, and

the external iliac, obturator, hypogastric, and ureteral groups. In 846 glands there was microscopical evidence of follicular hyperplasia in the inguino-femoral and pelvic glands, but fatty infiltration occurred more often in the external iliac group. There was a striking absence of lymph follicles in glands that had been subjected to heavy pre-operative irradiation. Hyaline degeneration was common in all glands. Nine cases of carcinoma of the cervix showed endometriosis in the lymph glands, which might be explained by blockage of the cervical canal with open lymph channels above the block. The lymph glands contained metastases in 46 per cent of vulval cancers, most commonly the inguino-femoral chain, and in 35 per cent of group II cervical cancers, most commonly the hypogastric glands.

Clinical Picture

Complicating pregnancy. The rare complication of pregnancy by carcinoma of the cervix in a primigravida aged 22 was reported by S. Goldstein. A patient, 6 months pregnant, was admitted to hospital with painless bleeding following coitus. Her menstrual history was normal and there was not any family history of cancer or tuberculosis. The abdomen was enlarged to the size of a 6-months pregnancy, and per vaginam there was a soft, friable, vascular mass, the size of a lemon, attached by a short pedicle to the anterior lip of the cervix. This was successfully removed with the cautery. A week later she was delivered of a macerated foetus. Deep X-ray therapy was given a fortnight after the confinement, and 3 months later she received radium treatment 3,600 mg. hours. Vaginal examination 4 months later showed a well healed cervix and a normal pelvis. Microscopically the growth was an adenocarcinoma with areas resembling sarcomatous change.

Treatment

X-irradiation.—W. Clarkson and A. Barker state that radium is so often misused in the treatment of carcinoma of the cervix that the number of patients who are thereby rendered incurable is far greater than the number cured by radium therapy. They further state that the 5-year survival rate of all cases of cervical carcinomas treated to-day does not exceed 10 per cent, yet 5-year survivals of well over 50 per cent may be obtained by the proper use of external irradiation followed by proper intracavitary irradiation.

Although it is recognized that the treatment of carcinoma of the cervix presents special difficulties in regard to dosage, M. C. Tod and W. J. Meredith feel that they have worked out a dosage system which is peculiarly adapted to that condition. The essential point of any such system, if useful, is that it ensures the application of a relatively homogeneous dose of radiation to the zone of tissue selected for treatment, the dose being expressed in rontgens delivered in a certain time period. The treatment zone must be defined, anatomical variations of the organ must be considered, and the type of intracavitary applicators and assessment of dosage described.

Two particular areas are noted at which dosage may be measured. The first is Point A which is 2 cm. lateral to the central canal of the uterus and 2 cm. from the mucous membrane of the lateral fornix in the axis of the uterus in the 'paracervical triangle'; and the second is Point B, the lymph node on the lateral pelvic wall, usually called the obturator node, 5 cm. from the midline. The dosage at Point A gives an average figure for the dosage received throughout a considerable zone in the paracervical triangle. Point B, the lymph node, is so frequently involved that this area should receive a lethal dose, and the radium should be so placed as to obtain the highest proportional depth dose. The limiting tolerance at Point A and the desirability of a sufficient dose at Point B are stressed.

Special applicators, which are made of rubber and are in three sizes, called vaginal ovoids, are used with this method, the shape ensuring an homogeneous dose over the whole surface of the ovoid. It is essential that the largest possible size be used. The calculations for dosage are based on a geometrical basis, and the Sievert formula is used. Treatment of the whole length of the uterine canal is strongly advised. The technique involves the use of two ovoids placed one in each lateral fornix, with a spacer or washer between them, and the knee-chest position is specially recommended for their insertion. Immediately after placing the ovoids in position a radiological examination should be made to ascertain if the radium is in a reasonably good position. A dose of 7,200 r. in 10 days is believed to be adequate for Point A, but the ideal dose at Point B remains to be determined. The relation of the system to the Paris and Stockholm techniques is discussed.

Acetone as haemostatic.—L. A. Pomeroy discusses the use of acetone for local bleeding as an aid to irradiation of the cervix in the treatment of carcinoma. This

therapy may be carried out in the operating theatre or merely with the patient in bed at home with the hips elevated; a short tubular speculum is inserted into the vagina, and 30 to 60 c.cm. of acetone are poured into it so as to come into contact with the cervix. After 10 minutes the original acetone is sponged out and fresh acetone applied. After a further 20 minutes this is also sponged out, fresh acetone being again applied for yet another 10 minutes. This treatment may be repeated 2 or 3 times daily for several days if necessary.

Clarkson, W., and Barker, A. (1938) *Radiology*, **31**, 729.

Goldstein, S. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 514.

Pomeroy, L. A. (1939) *Amer. J. Roentgenol.*, **41**, 73.

Strachan, G. I. (1939) *Proc. R. Soc. Med.*, **32**, 573.

Taussig, F. J. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 819.

Tod, M. C., and Meredith, W. J. (1938) *Brit. J. Radiol.*, **11**, 809.

UVEAL TRACT DISEASES

See also Vol XII, p 495.

Angioid Streaks

E. L. Goar reported a case of angioid streaks in the fundus associated with traumatic rupture of the choroid. The streaks appeared around the disc as small serrated lines of a light brown colour lying beneath the retinal vessels. These lines were narrower than the vessels. There was haemorrhage near the maculae of both eyes. There was no sign of any general disease, and no family history of eye afflictions. The aetiology of these streaks is unknown.

Goar, E. L. (1938) *Amer. J. Ophthalm.*, **21**, 907.

Ciliary Neuralgia

Treatment

W. Reitsch reported the occurrence of ciliary neuralgia, which manifested itself by great pain on closure of the eye and on ciliary pressure. Lateral movement of the eyeball also increased the pain. The author observed the coexistence of a painful area in the nasal mucosa in the region of the nasal bone. Touching this area with a larocaine plug resulted in cessation of ciliary pain. This is due to the fact that parts of the nasal mucosa are innervated by the anterior ethmoidal nerve which is a branch of the ophthalmic nerve, as is also the ciliary nerve. In all cases of intractable ciliary neuralgia the nasal mucosa should therefore be searched for painful areas and, if the 2 conditions co-exist, a larocaine plug will abolish the pain.

Reitsch, W. (1939) *Klin. Mbl. Augenheilk.*, **102**, 706.

VACCINIA AND VACCINATION

See also Vol XII, p. 515.

Subcutaneous Vaccination of Adults

M. Gherardini *et al.* examined 2,000 soldiers in whom subcutaneous vaccination was carried out. All the patients were 21 years old and the vaccine used was a dry vaccine diluted with physiological saline to 1:3200. Primo-vaccinates received 0.1 c.cm. and the reactions were rather marked, more so than in infants who reacted with few symptoms to subcutaneous vaccination. Re-vaccinates showed various reactions varying from mild to very strong. The strong reaction elicited in most primo-vaccinates indicates reduction of the dose. It is important to inject subcutaneously, and not into the muscular layer, as reactions tend to be more violent in the latter case. The extent of the reactions and the symptoms after subcutaneous vaccination indicate that this method, if suitable doses are given, is equal to intracutaneous vaccination. The method is preferable in districts where the population is not willing to undergo intracutaneous vaccination.

Gherardini, M., Kaiser, M., Hassmann, K., and Turk, I. (1939) *Med. Klin.*, **35**, 636.

VEIN DISEASES

See also Vol. XII, p. 526.

Varicose Veins*Treatment*

Allergic manifestations following injection treatment.—H. J. Shelley summarized the allergic manifestations sometimes encountered after the injection of varicose veins with quinine-urethane, sodium morrhuate, and monoethanolamine oleate (monolate). The reactions can be divided into 3 types: (i) erythema or urticaria; (ii) gastro-intestinal disturbances characterized by pain and diarrhoea, and (iii) cardiovascular disturbances sometimes leading to collapse and cyanosis. Shelley reported a case of the third type following an injection of monolate which ended fatally in spite of intravenous and cardiac injections of adrenaline hydrochloride. The patient had received 2 previous injections of sodium morrhuate and one of monolate with no ill-effects. To prevent the allergic reaction the patient may be desensitized before treatment begins. If a reaction occurs this therapy should be promptly suspended and immediate treatment of the symptoms instituted.

Ulceration

Treatment. R. R. Linton and J. K. Keeley discussed the 2 types of ulceration of the lower leg associated with varicose veins. The first type is the simple varicose ulcer due to incompetence of the saphenous veins. Obliteration by injection and/or ligation is adequate in the treatment of this type. The second type is the post-phlebitic ulcer developing from 1 to 20 years after a thrombophlebitis of the deep veins of the leg. This is not influenced by the normal varicose vein treatment. The authors devised a new method of treatment on the basis of the existing methods. The patient is first put into bed, the leg rested and the ulcer allowed to heal. Warm compresses of 2 to 4 per cent boric acid solution are applied to the ulcer every 2 hours. Skin grafting may be necessary or, if haemolytic streptococci are present, compresses of surgical solution of chlorinated soda to achieve this purpose. The next step is the ligation of the long saphenous vein at the sapheno-femoral junction in the groin. The sapheno-popliteal junction is ligated if the ulcer is on the postero-lateral surface of the leg. An ambulatory period of about 6 weeks follows this stage, an elastoplast bandage being applied to the whole limb. The next step is ligation of the communicating veins of the lower leg. This is performed under spinal anaesthesia as it may take a long time to find all the communications. In 41 cases thus treated 97.5 per cent resulted in complete cure.

Kienapfel reported the use of pancreatic preparations by mouth in the treatment of varicose ulcers of the leg. In many conditions affecting the skin there is hyperacidity and gastric atony; this is manifested by acne, seborrhoeic eczema, herpes, urticaria, pruritus, and psoriasis. Patients with varicose ulcers of the leg were treated by the administration of pancreatic preparations. The result was a better assimilation of foodstuffs and consequently an improved functioning of the skin. As circulation improved, the ulcers cleared up without local treatment. The author recommended pancreatic preparations as a useful adjuvant to local therapy in varicose ulcers of the leg.

R. Leriche and F. Froelich described Leriche's method of treating resistant ulcers of the leg by intra-arterial injection of novocain (procaine hydrochloride) solution. This treatment gave results similar to those from peri-arterial sympathectomy. The reason for this treatment was that, in old-standing ulcers of the leg, it was necessary not only to produce cicatrization but above all to sterilize the base and the surrounding skin area which is always grossly infected and a breeding ground for streptococci, staphylococci, *Bact. coli-communis*, and other organisms. The repeated injection of novocain into the femoral artery, 5 c.cm. at a time, for a few days produced astonishing results. The side-effects were a feeling of heat, hypotonia, and an increase of frequency, all of which were transient, and were well tolerated by the patients.

Bonnet summarized his experience during 2 years with the treatment of non-healing ulcers, especially of the leg, by the subcutaneous injection of novocain into their periphery. In every case a Wassermann test excluded syphilitic origin, and X-ray examination excluded bony attachment. All other methods of treatment were tried and, after they had failed, 8 to 12 c.cm. of novocain solution were

injected, every second day for 6 or 7 times, into the periphery of the ulcer. The results were excellent, and ulcers resisting all previous treatments healed within 15 days.

Bonnet (1939) *Rev. chn. Paris*, **58**, 443

Kienapfel (1939) *Dtsch. med. Wschr.*, **65**, 867.

Leriche, R., and Froelich, F. (1939) *Mém. Acad. Chn.*, **65**, 750.

Linton, R. R., and Keeley, J. K. (1939) *Amer. Heart J.*, **17**, 27.

Shelley, H. J. (1939) *J. Amer. med. Ass.*, **112**, 1792.

Thrombophlebitis

Following Sleep Therapy

H. A. Palmer gives case reports of 4 patients, 3 of whom were over 50 years of age and one 38 years, in whom thrombophlebitis occurred as a result of a course of sleep treatment. In the first 3 cases medinal (barbitone-sodium) and paraldehyde were used, and in the fourth case somnifaine and paraldehyde. It is emphasized that, although 3 cases were over the safety age of 55, there was no feature in the fourth case which might have served as a warning. The suggestion is made that all patients receiving similar treatment should be given a small dose of potassium citrate. In addition to daily exercises, vigorous massage should be applied to the lower limbs. Should this complication occur, rest and the application of heat with belladonna are indicated. Sulphanilamide may be used with advantage.

Treatment

Mecholyl iontophoresis—R. A. Sokolov and M. P. Meyers treated 19 cases of deep thrombophlebitis and 13 cases of chronic leg ulcers of various aetiology with mecholyl (acetyl-*i*-methylcholine chloride) iontophoresis. Improvement was recorded in all but one case. This substance has a vasodilator action similar to that of acetylcholine.

Post-Operative

Treatment.—N. W. Barker and V. S. Counseller found that post-operative thrombophlebitis occurred in approximately 1.6 per cent of patients who underwent laparotomy. They advise, in the acute stages of iliac and femoral thrombosis, elevation of the leg to an angle of 30° from the horizontal with continuous hot wet packs applied from the foot to the groin, both of which measures should be continued until the patient's temperature has remained normal for 4 days, until all swelling and oedema have disappeared from the leg below the knee, and until all pain and tenderness have vanished from Scarpa's triangle. The authors found that 10 to 18 days is usually sufficient for this and consider that prolonged recumbency favours atrophy of the muscles of the leg. The wearing of a heavy pure rubber bandage applied from the toes to the knee throughout the convalescence and for some months after is recommended. This should be applied over a long cotton stocking and retained while it is found that oedema develops after activity when it is not used.

Barker, N. W., and Counseller, V. S. (1938) *Proc. Mayo Clin.*, **13**, 785.

Palmer, H. A. (1939) *J. ment. Sci.*, **85**, 276.

Sokolov, R. A., and Meyers, M. P. (1939) *Amer. Heart J.*, **17**, 316.

Thrombosis

Multiple Thromboses

H. A. Derow *et al.* recorded a case of old recanalized and fresh fibrin thrombi in the inferior vena cava, and in the renal, portal, and splenic, and the proximal portions of the mesenteric and the peritracheal veins. The patient, a boy aged 15, presented the clinical picture of nephrosis, and pyelograms taken after intravenous injection of diodrast suggested polycystic disease of the kidneys. Death, due to pneumococcal peritonitis, occurred in coma. The kidneys were enlarged, but the renal pelvis were not dilated; microscopically the renal tubules showed slight cloudy swelling and oedema of the interstitial tissue, and normal glomeruli. Both renal veins were occluded from their junction with the inferior vena cava to the hila of the kidneys; the branches of the renal veins were patent. This was an extremely difficult, and fortunately very rare, condition.

So-called Traumatic Thrombosis of Axillary and Subclavian Veins

E. Roelsen observed 7 patients with a form of venous stasis of the upper extremity. The general symptoms were acute swelling of the arm, dilatation of the superficial veins of the arm and pectoral region, and pain corresponding to the axillary vein; there was a history of unaccustomed or severe muscular work with exacerbation of symptoms if the work was resumed. The chief symptom was venous stasis, the radial pulse being normal. After describing the symptoms and treatment in his 7 cases, the author discusses the differential diagnosis of the disease. There is always the possibility of the so-called scalenus anticus syndrome, characterized by reduced blood supply to the upper extremities due to anomalies of insertion of the scalenus anterior muscle (pressure of first rib). There is, however, no venous stasis in that syndrome. The symptoms suggested also traumatic venous thrombosis with venous stasis as the main symptom. There was, however, no difference in the venous pressure of the arms, such a difference being significant of traumatic venous thrombosis. The author is of the opinion that the disease is caused by a trauma due to over-exertion, perhaps with a predisposing factor (infection or pre-existing changes of the vein wall). The trauma together with the pre-disposing factor cause a spasm and this again causes the venous stasis. Formation of a thrombus is a secondary effect. The prognosis of the disease is good. If conservative treatment (rest, elevation of arm, compresses) is of no avail, operation should be tried. Venolysis with denudation of a portion of the vein will often help, if it does not, a piece of the axillary vein should be resected.

Post-Operative

Prevention C. H. Best reviewed the methods of preparation of heparin. The anticoagulant action of heparin is apparently due to its combination with the anti-thrombin of the serum. The best method of administration was found to be a small intravenous dose followed by constant intravenous injection to keep the clotting time at any chosen level. Experimentally heparin was found to prevent thrombus formation after veins had been mechanically or chemically injured. It also prevented the formation of white thrombi in monkeys, dogs, and cats. Experiments have shown that the increased clotting time in anaphylactic and peptone shock is probably due to the liberation of heparin. Owing to the indiscriminate selection of cases the value of heparin in preventing the clinical formation of thrombi is not yet certain. It is, however, established by the use of heparin in over 400 patients that it can safely be given to human subjects provided that during its preparation it has been through the stage of the barium salt.

C. Crafoord reported on the post-operative use of intravenous injections of heparin in the prevention and treatment of post-operative thrombosis, 50 to 100 mg. of heparin were injected 4 to 6 times daily and the coagulation time was determined frequently. A 5 per cent sterile neutral solution containing 0.25 per cent of trieresol was used and altogether 135 cases were treated. The results obtained have established the fact that heparinization definitely marks an advance in the post-operative prevention of thrombosis, and the authors suggested that injections should be given in every case in which this complication might occur.

Best, C. H. (1939) *Proc. Mayo Clin.*, **14**, 81.

Crafoord, C. (1939) *Acta chir. scand.*, **82**, 319.

Derow, H. A., Schlesinger, M. J., and Savitz, H. A. (1939) *Arch. intern. Med.*, **63**, 626.

Roelsen, L. (1939) *Acta med. scand.*, **98**, 589.

VERTIGO

See also Vol. XII, p. 544.

Ménière's Syndrome*Morbid Anatomy*

C. S. Hallpike and H. Cairns described the morbid changes found in the temporal bones of 2 patients suffering from Ménière's syndrome. Gross distension of the endolymph system and degenerative changes in the sensory elements were present. The authors suggested that the dilatation of the endolymph system is due to faulty absorption of the endolymph and consequent increase in pressure. When fully distended the endolymph system can no longer expand, if there are rises of pressure.

within it. The attacks of vertigo were thought to be initiated by a small rise of pressure in the labyrinth pressing on the end-organs of the labyrinth and producing a transient asphyxia.

Hallpike, C. S., and Cairns, H. (1938) *J. Laryng.*, **53**, 625.

Treatment

Injection of Alcohol

A. J. Wright's technique for the destruction of the labyrinth in the treatment of vertigo is as follows: under general anaesthesia, one minim of absolute alcohol coloured with methylene blue was injected through the oval window by perforating the footplate of the stapes. The treatment could be repeated if necessary. This treatment was chiefly applicable in (i) the aged in whom the radical removal of focal infections was attended by special risks, and (ii) cases of chronic labyrinthine disturbance due to middle-ear suppuration, particularly after radical operation on the middle-ear spaces.

Wright, A. J. (1938) *J. Laryng.*, **53**, 594.

VITAMINS

See also Vol. XII, p. 570, and Cumulative Supplement, Key Nos 1601-1609.

Vitamin A

Physiology

Concentration in blood—On the assumption that carotene is converted into vitamin A by the body, S. W. Clausen and A. B. McCord, studied the concentration of the carotinoid pigment and of vitamin A in the blood. Since the blood-cells contain little, if any, carotinoid, the analyses were made upon serum or plasma. The authors found that relatively large amounts of carotene and xanthophyll may pass through the placenta to the foetus. Vitamin A probably also passes through the placenta, but the foetus may also be able to form vitamin A from carotene. Carotene is readily absorbed from the diet, but the rate of absorption is slower than the rate of absorption of vitamin A. The low carotinoid content of the diet in early infancy and in the winter months explains the lower concentration of carotene and xanthophyll in the winter and in the first 6 months of life. Infection causes a prompt and considerable fall in the concentration of carotene, xanthophyll, and vitamin A in the plasma. This fall is due, in part, to low intake during infection, but also in part to fever. A few days after the temperature becomes normal, the vitamin A content of the plasma may rise considerably above normal. In severe untreated diabetes mellitus the tissues may not be able to metabolize carotene rapidly. In nephrosis and in severe chronic nephritis hypercarotinaemia may occur without xanthosis cutis. In Bright's disease the level of plasma vitamin A may be greatly elevated, probably because the liver fails to store it. In hypothyroidism the carotinoids of the plasma may be elevated and the vitamin A low. Successful treatment with thyroid corrects the anomaly. In coeliac disease the carotinoids and vitamin A are not readily absorbed.

Quantitative Requirements

L. E. Booher *et al.* investigated the vitamin A requirements of 5 normal adults. Each subject was kept on a diet adequate in all essentials and vitamins, except vitamin A, of which not more than 103 international units were included daily. After intervals of 16, 27, 29, 39, and 124 days respectively, signs of impaired dark adaptation were revealed as the earliest ocular abnormality. It was found that, in order to correct this impairment and maintain normal dark adaptation, vitamin A (in the form of cod-liver oil) was necessary in amounts of 25 to 55 international units per kilogram of body-weight. The daily requirements of carotene (expressed in terms of international units of vitamin A) for the same purpose varied between 43 and 103 units per kilogram of body-weight. Unit for unit the carotene in cotton-seed oil was about 50 to 60 per cent as effective in supporting normal dark adaptation as vitamin A in the form of cod-liver oil.

Toxicity

E. B. Vedder and C. Rosenberg conducted a series of experiments with rats to

determine the toxicity of vitamin A, using jewfish oil owing to its high vitamin A content. It was concluded that only doses in excess of 100,000 international units could produce toxicity in 50 g. rats, and that a factor of the oil other than vitamin A was responsible for the greater part of the toxicity observed. When vitamin D was given in conjunction with jewfish oil, but in a lesser proportion than the vitamin A content, it decreased the toxic effect. When the number of units of vitamin D exceeded those of vitamin A, the combination was much more toxic than the same amount of vitamin A alone. Vitamin B₁ afforded no protection against the toxicity of jewfish-liver oil administered to rats. The most striking results, however, were given by the administration of vitamin C, 5 mg. given daily protected all rats receiving such doses as 100,000 international units of vitamin A; 11 out of 12 rats receiving this therapy lived for 100 days (the time of the experiment), and grew normally.

Hypovitaminosis A

Association with endocrine disorders - M. G. Wohl and J. B. Feldman investigated the occurrence of vitamin A deficiency in 59 cases of various endocrine diseases. Of the methods for detecting vitamin A deficiency—the colorimetric for its estimation in the blood, the spectroscopic, and the dark adaptation—the last was employed. Physiologically, exposure to sunlight, before entering a dark room, is followed by inability to see, but after a time vision improves as the visual purple undergoes regeneration, which mainly depends upon vitamin A. The tests were carried out in a dark room with the pupils of the subject contracted by pilocarpine or eserine; each one was pre-exposed to a uniform light of known intensity for 3 minutes to bleach the visual purple, then the light was extinguished, and the light thresholds taken at 3- to 5-minute intervals, for half an hour or more. In 26 subjects with pituitary or adrenal disorders the results with the dark-adaptation test were so variable that no deductions were justified. Of the remaining 33 cases, which admittedly are rather few to justify conclusions, there were 20 with toxic goitre, and the results of the dark-adaptation test led to the conclusion that thyrotoxicosis rapidly destroyed and depleted the reserves of vitamin A in the body. In 4 myxoedematous and 3 post-operative hypothyroid patients the pathological results of the test suggested that a want of thyroxine was responsible for a failure in the conversion of carotene into vitamin A.

Sjogren's disease - The main symptom of Sjogren's disease, as first described in 1933, is dryness of all mucous membranes, especially a kerato-conjunctivitis sicca or keratitis filiformis. There is a complete absence of tears, rhinitis sicca with changes in the sense of smell, xerostomia, pharyngo-laryngo-trachetis sicca, lack of perspiration, achylia gastrica, and disturbed carbohydrate metabolism. According to W. Stahel the disease is mainly observed in women of post-climacteric age, who are very weak, have a severe atrophy of muscles, and often a chronic polyarthritis. It has been thought that the disease might be caused by a glandular infection, a disturbance of the haemopoietic apparatus, or some endocrine disturbance. The author is convinced from the results of therapy that the disease is caused by a lack of vitamin A. He gave 16,000 units of vitamin A daily and found that the symptoms disappeared.

Booher, L. E., Callison, E. C., and Hewston, E. M. (1939) *J. Nutrit.*, **17**, 317.

Clausen, S. W., and McCoord, A. B. (1938) *J. Pediat.*, **13**, 635.

Stahel, W. (1938) *Helv. med. Acta*, **V**, 5. Abstracted in *Med. Klin.* (1939), **35**, 557.

Vedder, E. B., and Rosenberg, C. (1938) *J. Nutrit.*, **16**, 57.

Wohl, M. G., and Feldman, J. B. (1939) *Endocrinology*, **24**, 389.

Vitamin B₁

Physiology

Excretion of vitamin B₁ - J. Marrack and H. F. Hollering demonstrated the excretion of aneurin (vitamin B₁) by 8 normal males and one normal female after intramuscular injection of 3 mg. of aneurin, and by one normal male after injection of 10 mg. All the subjects were eating a mixed, varied, and abundant diet. The urines were collected during 3-hour periods after injection. In 6 cases urine was collected during similar periods on another day when no aneurin was injected. Aneurin was excreted rapidly in the first 3 hours after injection; in the second 3-hour period there was a relatively small increase over the amount passed in control

periods. The amounts excreted per hour during the first 3 hours after injection of 3 mg. were in all cases much higher than after 1 or 2 mg. taken with food. One patient excreted 41 per cent of the injected dose in 3 hours. A certain amount of the aneurin must be excreted by the kidneys before there is time for it to be stored in the body. There appears to be no relation between the volume of urine and the amount of aneurin excreted.

Therapeutic Applications

Nervous disorders.—N. Holmin treated 21 patients with various nervous disorders by intramuscular injections of vitamin B₁; each injection corresponded to 20 mg. of crystalline aneurin chloride and injections were given once daily. No ill effects were observed. The treatment showed the following results: of 12 cases of Parkinsonism, 2 were improved, 3 somewhat favourably influenced, and 7 showed no improvement. The improvement consisted in changes of the speech, better articulation, disappearance of the greasiness of the face, and decrease of tremor and rigidity. Of 3 cases of neuralgia: 2 improved (1 diabetic and 1 adipose and polyarthritic woman). There were 2 cases of neuritis or possibly myelitis associated with achylia, both of which were improved considerably and showed disappearance of paraesthesia of the legs. Of 3 cases of disseminated sclerosis, 2 improved with decrease of tremor and spasm and disappearance of constipation. One case of spastic paraplegia, after 3½ months of vitamin B₁ treatment, showed return of motility and disappearance of headaches.

Pain of ischaemic origin—M. Naide treated rest pain of ischaemic origin with large doses of vitamin B₁, because it is essential for tissue metabolism and because lack of it causes neuritis and pain. It was presumed that the pain in ischaemic conditions was due to the poor blood-supply to the part resulting in a poor supply of vitamin B₁. Ten patients with ischaemic neuritis were given doses of 100 mg. of vitamin B₁ intravenously. Seven were completely relieved, 2 partially relieved, and one obtained no relief from the pain. It was necessary to keep the patients on a maintenance dose of 20 to 100 mg. once or twice a week during the time the vascular condition remained unchanged. Naide also considered it advisable to continue the usual methods of stimulating the peripheral circulation. The vitamin therapy had no effect on gangrene, ulcers, or objective neurological changes. Vitamin therapy was given with varying results to 2 patients with intermittent claudication. It was found useless in this series to give the vitamin by mouth, but there were no toxic effects from its intravenous administration.

Holmin, N. (1939) *Acta med. scand.*, **98**, 444.

Marrack, J., and Hollering, H. F. (1939) *Lancet*, **1**, 325.

Naide, M. (1939) *Amer. J. med. Sci.*, **197**, 766.

Vitamin B₂ Complex

Therapeutic Applications

Nicotinic acid in disturbed fat absorption—H. Siedek and I. Reuss reported the use of nicotinic acid in the form of nicotinamide in cases of disturbed fat absorption. This disturbance is often present, together with a disturbed carbohydrate metabolism, in conditions in which persistent diarrhoea is present. There is no apparent abnormality of the pancreas and the diastase level and blood sugar are normal. Patients with diarrhoea over a longer period somewhat resemble cases of sprue, which is known to have a connexion with pellagra. This led the authors to try the use of nicotinamide—the pellagra-preventing factor of the vitamin B₂ complex; 3 injections of 2 c.cm. of nicotinamide solution improved the patient's condition dramatically, and, after discharge from hospital, he was given injections twice weekly of 2 c.cm. of the preparation. His anaemia disappeared and in 3 weeks a complete cure was obtained.

Nicotinic acid in pellagra-like deficiency diseases.—J. V. Landor described 10 cases in Singapore of a vitamin B₂ deficiency disease characterized by scrotal dermatitis and/or angular stomatitis and soreness of the tongue which was not benefited by nicotinic acid therapy. The patients were given ten 0.05 g. tablets of nicotinic acid daily for 14 days. There was only very slight improvement in some cases, and many of the cases became worse. Treatment with marmite caused the mouth condition to heal completely in a few weeks and the scrotum to improve very much, though the skin did not regain its normal texture for some time. Landor therefore concluded that all pellagra-like deficiency diseases do not respond to nicotinic acid

treatment, but he described a case of classical pellagra which yielded to this treatment.

Landor, J. V. (1939) *Lancet*, **1**, 1368.

Siedek, H., and Reuss, L. (1939) *Wien klin. Wschr.*, **52**, 432.

Vitamin C

Physiology

Concentration in blood, and urinary excretion.—Three patients with vitamin C deficiency, as demonstrated by complete absence in the blood of this vitamin, associated with the haemorrhagic manifestations of scurvy, were treated with the monoethanolamine salt of ascorbic acid by E. L. Lozner *et al.* Tests were performed for individual tolerance, and comparisons made between oral, intravenous, and intramuscular treatment. The oral administration of 1 g. of vitamin C made little difference to the ascorbic acid blood levels, and no excretion occurred in the urine. One gram of vitamin C dissolved in isotonic salt solution, and given intravenously, caused a rapid rise in the blood level, followed by marked excretion in the urine. When 1 g. of the monoethanolamine salt of ascorbic acid was injected intramuscularly the blood-level rise was less dramatic, and the excretion in the urine considerably less than with the intravenous injection. In both instances excretion was highest in the first 5 hours. One of the patients who showed a marked vitamin C deficiency was saturated with 100 mg. of the monoethanolamine salt daily, with a resulting rise from 0.12 to 0.81 mg. per 100 c.cm. of blood plasma. There were no unpleasant reactions in any of the cases.

Quantitative Requirements

H. Rietschel and J. Mensching found that the diseases due to lack of vitamins in animals were very different from symptoms due to lack of vitamins in man, and they therefore began observations on man. A diet free as far as possible from vitamin C was given for 100 days in one case. During and after the 100 days there were no morbid symptoms with the exception of a cold which was cured in 4 days without treatment. The weight of the patient increased from 89 kilos to 94.5 kilos. The vitamin C content of the blood decreased from 0.72 mg. per 100 c.cm. on the first day of the experiment to 0.06 mg. per 100 c.cm. on the hundredth day. Reducing substances in the urine (not necessarily ascorbic acid) amounted to 1 mg. per 100 c.cm. as compared with the normal 2 to 3 mg. per 100 c.cm. The authors concluded that the requirements of vitamin C were very small, because vitamin C, when used up (oxidized), is reduced and used again. It is possible that other reducing substances may take the place of vitamin C in an emergency. There is also the possibility that vitamin C is synthesized in the organism.

M. Heinemann points out that there are widely different requirements of vitamin C both for complete saturation and for protection against scurvy. For this latter purpose 0.4 mg. of ascorbic acid per kg. of body weight, or even less, appears sufficient, but at least 0.8 mg. per kg. is used daily by healthy saturated subjects. Active tuberculous patients require abnormally high amounts, although it is observed that high requirements are not specific for this disease. Tuberculosis may be said to predispose towards scurvy because of the increasing requirements for vitamin C. Patients with peptic ulcer show a low concentration of ascorbic acid in the blood; this is obviously due chiefly to the dietary treatment which fails to provide a sufficient supply of vitamin C.

Detection of Hypovitaminosis-C

The intradermal dye test.—H. G. Poncher and C. H. Stubenrauch investigated the efficiency of the intradermal dye test for the determination of vitamin C deficiency. The test depends upon the decolorization of a blue dye to its leuco form in the presence of vitamin C. The rate of decolorization depends upon the amounts of ascorbic acid in the tissues. The authors treated 41 subjects, 6 suffering from clinical scurvy, 9 with a low ascorbic acid blood-level, and 26 normals. In the first group the decolorization time averaged 5.8 minutes, in the second 9.4 minutes, and in the normal group 7.6 minutes. Their observed times for bleaching of the dye did not agree with other observers, and they found a lack of correlation between the decolorization time and the level of ascorbic acid in the blood. They therefore concluded that the test was not reliable, and that the dye was probably bleached by other agents in the skin.

Therapeutic Applications

I. S. Wright discussed various indications for administration of ascorbic acid. Vitamin C deficiency occurred when intake of the substance was apparently adequate, in increased metabolism (with or without pyrexia), achlorhydria, colitis, and other intestinal disturbances. When the intake of vitamin C was insufficient, deficiency inevitably occurred as man is unable to synthesize this substance, and his storage capacity is limited. A marked deficiency of the vitamin existed in such conditions as pneumonia, tuberculosis, rheumatic fever, whooping-cough, and osteomyelitis, and it was suggested that the vitamin C content of the tissues should be kept up to normal as a matter of supporting therapy. Evidence accumulated that citrus fruit, and other foods possibly contained ingredients which were absent in synthetic preparations of ascorbic acid and, when possible, use of the natural source seemed advisable. The curative and maintenance dosage of ascorbic acid varied between 30 and 50 mg. by mouth daily. Quantities up to 100 mg. were given intramuscularly each day, though doses up to 1,000 mg. in some cases failed to cure scurvy.

In gold therapy reactions.—In 3 patients, under treatment with gold injections, A. Sande found various symptoms, such as haemoptysis, petechiae, and urobilinogenuria. Vitamin C in doses of 100 to 200 mg. injected intravenously removed the symptoms. Experiments on guinea-pigs showed that injection of gold preparations diminished the number of leucocytes in the blood and reduced the amount of ascorbic acid (vitamin C) in the tissues. The ascorbic acid content of the liver tissue, however, remained at a normal level. The diet of the animals contained a considerable amount of vitamin C, in spite of which these changes occurred. The greatest reduction of the vitamin C content was obtained when the gold preparations were injected intravenously.

Hennemann, M. (1938) *J. clin. Invest.*, **17**, 671.

Forner, F. I., Pohle, F. J., and Taylor, F. H. L. (1939) *New Engl. J. Med.*, **220**, 987.

Poncher, H. G., and Stubenrauch, C. H. (1938) *J. Amer. med. Ass.*, **111**, 302.

Rietschel, H., and Mensching, J. (1939) *Klin. Wschr.*, **18**, 273.

Sande, A. (1938) *Klin. Wschr.*, **17**, 1762.

Wright, I. S. (1938) *Ann. intern. Med.*, **12**, 516.

Vitamin K

Therapeutic Applications

J. D. Stewart investigated the prothrombin deficiency and the effects of vitamin K in obstructive jaundice and biliary fistula. It has been shown that lack of fat-soluble vitamin K leads to haemorrhage and that this vitamin is not absorbed from the intestine in the absence of bile salts, and that in the absence of this vitamin there is a deficiency of prothrombin in the blood. If the plasma prothrombin concentration is less than 50 per cent of normal, dangerous haemorrhage may occur. Thirteen patients suffering from obstructive jaundice in some form of liver damage were found to have a low prothrombin level which, on treatment with vitamin K and bile salts, rose on an average 32.8 per cent. The level of the plasma prothrombin depends upon liver function as well as on the absorption of vitamin K, and it may drop still further after operation on jaundiced patients, if the condition is not treated.

G. H. Scanlon *et al.* reported a case of post-operative bleeding in a jaundiced patient in whom the treatment raised the blood-prothrombin level. Vitamin K is of no use in the treatment of purpura and haemophilia as the blood prothrombin is normal in these conditions. The prothrombin level was slightly reduced in 3 cases of acute leukaemia and greatly reduced in Laennec's cirrhosis which is not, however, influenced by vitamin K, as the reduction is due to defective liver function and not to deficient absorption of the vitamin.

Vitamin K has proved successful in reducing the time of prothrombin-clotting and blood-clotting in the newly-born. Observations were made by W. W. Waddell and D. Guery on 10 cases, with 10 controls. One c.cm. of vitamin K concentrate was administered orally at the end of 24 hours, 0.5 c.cm. at the end of 48 hours, and 0.5 c.cm. after 72 hours. It was found that the prothrombin- and the blood-clotting times of untreated infants varied individually and from day to day, but for the most part the longest time needed for clotting occurred at 48 to 72 hours after birth. No unusually high rates were observed after the sixth day. This fact

was supported by the rare occurrence of haemorrhagic disease after the fifth day of life. Among treated infants a low uniformity was observed, the longest prothrombin-clotting time being 40 seconds. In 2 cases of the newly born in whom the prothrombin-clotting time was found to be $5\frac{1}{2}$ minutes and 7 minutes respectively, and the coagulation time 8 minutes and 11 minutes, administration of vitamin K within 2 hours reduced these levels to 40 seconds and 5 minutes in the first case and 55 seconds and 4 minutes in the second case. The value of these investigations is emphasized by the experience of Grulee and Bonar who find that the mortality-rate of the newborn from intracranial haemorrhage may be as high as 1 in 25 or as low as 1 in 150 deliveries.

Scanlon, G. H., Brinkhaus, K. M., Warner, E. D., Smith, H. P., and Flynn, J. E. (1939) *J. Amer. med. Ass.*, **112**, 1898.

Stewart, J. D. (1939) *Ann. Surg.*, **109**, 588.

Waddell, W. W., and Guerry, D. (1939) *J. Amer. med. Ass.*, **112**, 2259.

Vitamin P

Therapeutic Application

In haemorrhage --The effect of hesperidin, vitamin P of Szent-Gyorgyi, on capillary fragility was the subject of a study by H. Scarborough and C. P. Stewart. The oral administration of 1 g. daily succeeded in reducing the number of haemorrhages in 6 patients with vitamin deficiency. Its effect was observed when petechial haemorrhages were induced by a positive-pressure method, and with spontaneous haemorrhages following injections of arsenic or bismuth.

Scarborough, H., and Stewart, C. P. (1938) *Lancet*, **2**, 610.

VOMITING

Epidemic Nausea and Vomiting

J. D. Gray described an outbreak of epidemic nausea and vomiting in a school in South Hampshire at the end of 1938, similar to an occurrence in the Isle of Thanet described by Miller and Raven in 1936. The illness was short, lasting about 6 days. The patients complained of vertigo, nausea, and vomiting. The condition was usually nonfebrile. Frontal headache and occasionally bradycardia were noted. Diarrhoea was frequent. The best description given by the patients themselves was that they felt 'sea-sick'. Food, milk, and drains were all examined and absolved from suspicion as possible causes of the outbreak. Evidence suggested that the condition was very probably an acute infection of the central nervous system, possibly of a virus type, with an incubation period of 2 days. The mode of spread may have been by droplet infection. The attacks were presumably not isolated incidents; much more probably the infection was kept alive by sporadic cases occurring throughout the country, and only assuming epidemic proportions when the environment was favourable. The importance of this disease is the possibility of its confusion with blood-poisoning or Sonne dysentery.

Gray, J. D. (1939) *Brit. med. J.*, **1**, 209.

Treatment

Sodium chloride

A. Ravina described a simple method of treating nausea and vomiting. The ingestion of salt-water, as practised by various Australian doctors prevented, in their view, severe damage due to long exposures to the sun and prolonged marches. It was also suggested by a few that salt-water was a very good preparation for athletes, especially cross-country runners. Ambard recently introduced the administration of sodium chloride in incessant vomiting following operations, with very good results. In a small child suffering from violent diarrhoea and vomiting ingestion of one glass of salt-water (5 per cent sodium chloride) stopped the symptoms in 10 minutes. The author suggested a dose of 20 to 60 gr. of salt to a tumblerful of water. The action is attributed to the effect on the nervous system.

Ravina, A. (1939) *Pr. méd.*, **47**, 907.

VULVA AND VAGINA DISEASES

See also Vol. XII, p. 606, and Cumulative Supplement, Key Nos. 1610-1612.

Vulva*Leucoplakia Vulvae*

Treatment.—The treatment of 4 cases of leucoplakia vulvae is reviewed by A. H. Kevorkian. He advocates the local application of a strong solution of oestrogen in the form of 60,000 units of oestradiol per c.cm. of sesame oil. This treatment was found effective in healing the excoriations and lesions of the affected areas and in relieving the pruritus. Initial injections were performed at 2 to 6 day intervals, 1 c.cm. of the preparation being used. When the pruritus had been controlled, the patient applied a small amount daily in the form of a salve.

Kevorkian, A. H. (1939) *New. Engl. J. Med.*, **220**, 661.

Vagina*Absence or Obliteration of Vagina*

Surgical treatment. V. S. Counsellor reviewed the various operative procedures for the correction of congenital absence and traumatic obliteration of the vagina. The operation of choice is the McIndoe operation, a simple method of utilizing a large Thiersch graft taken from the thigh and implanting it into the vaginal position. The space between the bladder and rectum up to the reflection of the peritoneum is first opened. A Thiersch graft of sufficient size covers a rubber mould constructed to conform to the depth and diameter of the new vagina. The mould carrying the graft is then placed within the vaginal tract and secured firmly in this position for several weeks. Then, when the mould is removed, the vaginal canal is completely lined with a thin layer of epithelium, and closely resembles a normal vagina. In a few cases, contraction later produces some difficulty, but, in these, dilatation should be continued by the patient for a considerable time.

Vaginitis

Aetiology.—As the *Trichomonas vaginalis* is known to remain for long periods in the vaginal secretion without symptoms, and to persist after cure of the symptoms, G. Fielding Hibbert and F. H. Falls investigated the problems whether the trichomonas was the sole cause of the vaginitis, whether an independent organism was present and there was a symbiotic relation between it and the trichomonas, and whether patients harbouring the trichomonas and another organism but without symptoms had become immune to one or either of them. The organism isolated from their series was the *Streptococcus subacidus* of Holman, that it was pathogenic was shown by its fulfilment of Koch's postulates. It produced an immune reaction when injected intradermally. Local clinical improvement was more rapid and apparently more lasting when general antibody reaction was stimulated by a vaccine in addition to local antibody stimulation by means of a filtrate of the organism. The pH of the vagina was high when the streptococcus was present in large numbers irrespective of the presence or absence of the trichomonas. As symptoms ceased when the streptococcus disappeared and the trichomonas persisted, it appeared that the streptococcus was responsible for the morbid reactions.

Treatment.—F. B. Zener discussed a modification of vioform (iodochlorhydroxyquinoline) ointment treatment for *Trichomonas vaginalis* vaginitis in which the ointment is replaced by powder. The advantages are several. There is less soiling of the clothes, the cost of the therapy is small, and no toxic effects have been observed. The powder is combined with magnesium trisilicate which is a most efficient substance for rendering the vagina unfavourable to the trichomonas, by elevating the vaginal pH. The two powders are combined in the proportion of one part of vioform to 9 parts of magnesium trisilicate, approximately 50 gr. being used per treatment. This is carried out with an insufflator, 3 times a week. Of 140 cases treated, 137 were pronounced cured, with 3 relapses, but when vioform powder was given orally in four 4-grain tablets in addition to the vaginal insufflation, an entire group of 112 cases was cured, with no recurrences. The author feels that sufficient evidence is forthcoming to suggest the rectal origin of the parasite.

G. C. Shaufler *et al.* treated infections of the immature vagina with local applications and sulphanilamide. The injections were given for such conditions as gonococcal

endocervicitis and proctitis, *Trichomonas vaginalis* infections, discharges due to foreign bodies and worms, and cases complicated by pelvic infection. Ninety-nine cases were treated by silver nitrate ointment, 31 by vaginal application of amniotin (an oestrin preparation), and 19 with pyridium suppositories. Of these methods amniotin application was found to be the most satisfactory, but the time elapsing before cure was 8 weeks. Sulphanilamide was given in 261 cases and was not found very satisfactory in treating the vaginitis of children

Posterior Vaginal Hernia

F. F. Cary and E. L. Young reported a case of posterior vaginal hernia, a condition of which only 70 cases have been reported. The three main factors leading to the development of a vaginal hernia are weakness of the pelvic floor, and accidents of parturition; intra-abdominal pressure such as pregnancy, ascites, or tumours; and sudden trauma as in childbirth, straining, or lifting of weights. The condition must be differentiated from rectocele and uterine prolapse. The true posterior vaginal hernia is a definite peritoneal sac with a neck. The symptoms are a bearing-down feeling and the sensation of a mass in the vagina. When incarceration or strangulation of the intestine in the hernial sac has occurred, characteristic symptoms of obstruction are present.

Tumours

Primary carcinoma—F. V. Emmert analysed 37 cases of primary carcinoma of the vagina. The age incidence varied between 26 and 82 years, the commonest age being 45 to 60 years; 7 of the patients were nulliparous. The site most often affected was the posterior fornix. The tumour was of the squamous-celled type, either ulcerative or papillary, single in 24 cases and multiple in 13. Haemorrhage was reported in 31 cases and one patient noticed a blood-stained discharge after coitus. Of the 33 cases treated more than 5 years ago, only 4 have remained well, one after operation and three after radiation. It was suggested that in the early stages a radical operation should be performed, but that later cases should be treated by radium with or without X-ray therapy.

Melanoma—R. C. Nucci described a case of malignant melanoma of the vulva in a woman aged 76, who had always had a small mole on the right labium majus. She noticed painless black lumps on the right side of the vulva which 4 months later began to bleed and were considerably larger. The patient felt 'lumps' in the left groin 6 weeks before admission. On examination the vulval mass was somewhat nodular, the size of a tangerine, and purple in colour with several pigmented spots on the inner surface of the labium. There were large firm masses in both inguinal regions. Biopsy showed that the growth was a melanoma, it was then treated with radium, and again about one month later; but, as there was not any improvement in the general condition, the tumour was removed. She was temporarily more comfortable, but later developed a cough and pulmonary congestion and succumbed about 6 weeks after the operation, melanomatous metastases being found at necropsy in the lungs, stomach, and pancreas.

Cary, F. F., and Young, E. L. (1939) *New Engl. J. Med.*, **220**, 700.

Counseller, V. S. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 632.

Emmert, F. V. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 1058.

Hibbert, G. I., and Falls, F. H. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 219.

Nucci, R. C. (1938) *Amer. J. Obstet. Gynaec.*, **36**, 512.

Shauffer, G. C., Kanzler, R., and Shauffer, C. (1939) *J. Amer. med. Ass.*, **112**, 411.

Zener, I. B. (1939) *Amer. J. Surg.*, **44**, 416.

WHOOPING-COUGH

See also Vol. XII, p. 616.

Aetiology

Adult Carriers

D. Gajzágo and O. Göttsche called attention to the possibility of adults spreading whooping-cough, basing their observations on clinical histories in which the only possible contacts for children suffering from whooping-cough were adults; the

serological complement-fixation test confirmed this suspicion. The authors stated that adults can repeatedly contract whooping-cough, usually of a very mild form, in the course of which they disseminate Bordet-Gengou bacilli. The authors therefore insist on strict supervision of nurses engaged in nursing children suffering from whooping-cough. Nurses should wear a face-mask when nursing children, and their family histories should be carefully scrutinized. A half-yearly complement-fixation test should also be carried out, and every nurse should immediately report any cough or cold.

Gajzágó, D., and Gottche, O (1939) *Dtsch med Wsch.*, **65**, 875.

Bacteriology

From examination of the sera of 23 cases of whooping-cough, the clinical diagnosis of which had been confirmed by complement-fixation and agglutination tests, and in which pertussis vaccine had not been given, D. G. Evans and H. B. Matland found that pertussis toxin, which is extremely labile, was not antigenic. The necrotic effect of the toxin was not neutralized by the preliminary injection of convalescent pertussis serum.

Evans, D. G., and Matland, H. B. (1939) *J. Path. Bact.*, **48**, 465.

Complications

Convulsions

K. Habel and P. F. Lucchesi investigated convulsions complicating whooping-cough in 41 cases. They found that the chief predisposing factors were the severity of the paroxysm, cyanosis, broncho-pneumonia, congenital defects of the brain, and the age of the patient. Most of the convulsions occurred in patients under the age of 2 years. The convulsions were usually transient and indefinite without localizing neurological signs and were usually followed by vasomotor collapse. The cerebrospinal fluid was normal in most cases but a slight lymphocytosis, positive reactions to tests for albumin and globulin, and increased sugar content were the most constant changes encountered in others. The commonest morbid changes found at necropsy were congestion and oedema of the brain. The mortality rate for the series was 78 per cent, that of whooping-cough uncomplicated by convulsions being 5 to 10 per cent. In 17 patients who received blood transfusions the mortality-rate was only 35 per cent. Treatment was usually useless, but lumbar puncture without complete drainage, sedatives, and hypnotics were tried. The use of inhalation anaesthesia or morphine to overcome the convulsion was condemned as in this series the 6 patients who received this treatment all died.

Habel, K., and Lucchesi, P. F. (1938) *Amer. J. Dis. Child.*, **56**, 275.

Diagnosis

Discussing the diagnostic difficulties inherent in whooping-cough, A. B. Donald reports that, in a series of 171 cases sent to hospital as whooping-cough, 26 per cent were wrongly diagnosed, and 28 per cent which were bacteriologically confirmed as whooping-cough had not been heard to whoop before admission and never whooped in hospital. In view of this wide margin of clinical error, he endeavoured to assess the value of various methods of laboratory diagnosis.

(i) *Specific tests*. (a) The cough-plate method is the only means of certain diagnosis in the early stages. In a series of 134 cases, 10 per cent gave positive plates in the first week, 93.5 per cent in the second week, 94.8 per cent in the third week, 44 per cent in the fourth week, 7.1 per cent in the fifth week, and less than 1 per cent in subsequent weeks. Of 134 positive plates obtained at various stages of the illness, 70 per cent had an estimated pertussis colony count of 10 or less; the procedure may have value as indicating the cessation of activity; 110 cases were examined on the day of discharge or shortly before, and in no instance was a carrier found; 2 plates were taken from each patient. (b) The complement-fixation test is of little value in early diagnosis as it does not become positive until the third or fourth week or later. It may be used to establish the diagnosis in late or atypical cases when the period of expectoration of the bacillus is past. In a series of 123 cases the reaction became positive in 25 per cent during the third week and reached a maximum during the eighth week, when 89 per cent of the cases gave positive fixation reactions. (c) The intradermal test, in which a suspension of *Haemophilus pertussis* is used, is valueless in diagnosis. (ii) *Non-specific tests*: (a) The total leucocyte count

during the third and fourth weeks averages 30,000 per c.mm. with a differential count showing 65 per cent lymphocytes and 28 per cent polymorphonuclears. (b) The erythrocyte sedimentation rate is slightly retarded or normal in almost all uncomplicated cases of whooping-cough in the early stages, with a slight increase in the later stages of the illness.

Donald, A. B. (1938) *Brit med J*, 2, 613.

Treatment

Prophylaxis

Tests for susceptibility—M. K. Bazemore and J. C. Williams studied 79 children to determine the reliability of the intracutaneous tests for susceptibility to whooping-cough. They found that the tests gave no results of value. They were made both before and after immunization with pertussis vaccine but showed no specific correlation. Intradermal testing cannot be considered of value in detecting susceptibility or immunity to whooping-cough.

Vaccines M. Siegel investigated the prophylactic value of various whooping-cough vaccines on 1,270 children under 6 years of age in Brooklyn. This trial, in which vaccines were given for the 9 months, July 29th, 1935 to April 29th, 1936, was controlled by observation of 1,016 children from the same area and of the same age who had not had the disease. The vaccinated and control children were followed up until June 30th, 1937, from 14 to 23 months after vaccination. Of the vaccinated children 3.6 per cent contracted characteristic whooping-cough, compared with 4.2 per cent of the controls. Doses of 50 millions of bacilli or less seemed to have little, if any, prophylactic value, and this seemed to be also true of doses of 80 billion bacilli made from a very old stock strain. In 2 groups, comprising a total of 294 children inoculated with 80 billion bacilli of Sauer's vaccine or the vaccine of the New York Department of Health, no case showed characteristic whooping-cough, but they were not so much exposed to it as some of the other children. In general, symptoms developed almost as often among the vaccinated after known exposure as among the control children. It is extremely difficult to assess the prophylactic value of various vaccines as it is impossible to tell the degree of exposure to which the children have been subjected. This elaborate investigation into more than 2,000 children has therefore been inadequate to justify definite conclusions.

Curative

Vitamin C.—That the administration of vitamin C in whooping-cough has an effect upon the course of the disease is at present unproven, according to D. Gairdner. Otani had found that ascorbic acid, when added to a solid medium on which *H. pertussis* was grown, inhibited the growth of that organism and had reported favourable results in the practical application of his work. Gairdner treated 41 children with whooping-cough as out-patients, 21 of them being treated solely with large doses of vitamin C while the remaining 20 served as controls. They were seen as out-patients once a week. Only those whose cough was of less than 3 weeks' duration when first seen were included. The mothers were asked to note down on a form the number of paroxysms occurring during each separate day and each night, thus making the assessment of progress and of cure as objective as possible. When the night cough had ceased and the day cough had lost its paroxysmal character and become slight, the patient was discharged. The dosage adopted was: first week 200 mg. daily, second week 150 mg. daily, third and subsequent weeks 100 mg. daily, given in divided doses. Patients under one year of age were given half these amounts. In the 21 cases treated with large doses of vitamin C, the illness lasted 35 days. In those untreated the duration was 41 days, a difference lying within the limits of statistical error. The average gain in weight was the same in both groups. These figures were in keeping with the general clinical impression that there was no striking difference in the course of the disease in the 2 sets of cases.

Of Complications

Sulphanilamide.—A. R. Thompson and C. R. M. Greenfield assign an important role to the *Streptococcus pyogenes* as the secondary invader responsible for the more severe and common complications of measles and whooping-cough, especially complications affecting the middle ear and lungs. In an attempt to assess the value of chemotherapy in the prophylaxis and treatment of complications, a series of 1,219 cases of measles and 244 cases of whooping-cough was divided into two groups.

The first group, including a higher proportion of the more severe cases, received sulphanilamide or benzylsulphonamide from the time of admission, the dosage being graded according to age, and increased if any complications developed; the second group acted as a control. The first group developed fewer complications than the second, the difference being greatest in the aural sequelae of measles and the pulmonary complications of both diseases, results in both cases tending towards a reduced stay in hospital. The drug is well tolerated by children over the prolonged periods necessary for the results to be obtained. In treatment it gives encouraging results in young children, especially in broncho-pneumonia, otitis media, and the upper respiratory catarrhs. Sulphanilamide appears to be more effective than its benzyl derivative.

Vitamin D —F. Hansen laid stress on the importance of the greater susceptibility of the rachitic child to bacterial infections. Rachitic children with whooping-cough had a mortality thrice as high as that of otherwise normal children with that disease, and the duration of whooping-cough was 3 to 4 weeks longer in the rachitic than in normal children. After treatment with vitamin D the difference was remarkably reduced. The most frequent cause of death in whooping-cough was broncho-pneumonia, and, as rickets favoured the incidence of broncho-pneumonia, it increased the mortality in whooping-cough. The author determined the increase and decrease of agglutination for Bordet-Gengou bacilli in the serum, and found that the formation of agglutinins was retarded in rachitic children and that the amount of agglutinin was smaller than in normal children with whooping-cough. Vitamin D should be given to every infant in the first year of life with whooping-cough and to older children suspected of rickets.

Bazemore, M. K., and Williams, J. C. (1939) *Amer. J. Dis. Child.*, **57**, 1246.

Gairdner, D. (1938) *Brit. med. J.*, **2**, 742.

Hansen, F. (1938) *Munch. med. Wschr.*, **85**, 1949.

Siegel, M. (1938) *Amer. J. Dis. Child.*, **56**, 1294.

Thompson, A. R., and Greenfield, C. R. M. (1938) *Lancet*, **2**, 991.

YAWS

See also Vol. XII, p. 631.

Aetiology

Yaws as a Form of Syphilis

C. S. Butler argued that yaws was merely a form of syphilide common in all communities with a high incidence of syphilis and a low index of personal hygiene. If syphilis was ineffectively treated for generations, it eventually affected the whole population, not as a venereal disease but as one of the exanthemata of childhood. The disease became latent in most of the population and, although some might show osseous and mutilating lesions, nervous or vascular manifestations were very rare. The majority of the population remained free from symptoms. Attempts to find a different strain of *Treponema* to account for it were open to question as founded on insufficient data.

Butler, C. S. (1939) *Amer. J. clin. Path.*, **9**, 1.

YELLOW FEVER

See also Vol. XII, p. 660, and p. 145 of this volume.

Pathology and Morbid Anatomy

Brain Changes

L. D. Stevenson made a study of small pieces of brain tissue from 14 persons who died of yellow fever. There was marked perivascular haemorrhage in various parts of the brain in most of them. The findings were confirmed by the study of 20 whole brains. The haemorrhages were most frequently found in the subthalamic and periventricular regions at the level of the mamillary bodies. The temporal pole

and the cerebellum were frequently involved. Changes in the nerve cells were insignificant, and it was concluded that there was no definite evidence of neuro-tropism on the part of the virus of yellow fever in this series. The haemorrhagic conditions were considered to resemble those found in alcoholic encephalopathy, but were of greater severity.

Stevenson, L. D. (1939) *Arch. Path.*, **27**, 249.

Differential Diagnosis

Liver Changes following Burns

T. H. Belt described 4 cases of extensive superficial burns fatal within 4 days in which the liver showed severe changes indistinguishable from those in yellow fever. The liver cells had undergone mid-zonal necrosis, the cytoplasm contained peculiar rounded concentrations, 10 to 20 μ in diameter, Councilman's bodies, described by W. T. Councilman, and there were numerous and typical nuclear inclusions of the form described by E. V. Cowdry as Class A, which suggested a virus infection.

Belt, T. H. (1939) *J. Path. Bact.*, **48**, 493.

Councilman, W. T. (1890) *Report on Etiology and Prevention of Yellow Fever*, U.S. Marine Hospital Service.

Cowdry, E. V. (1934) *Arch. Path.*, **18**, 537.

Treatment

Combined Yellow Fever and Smallpox Vaccination

M. Peltier *et al* have combined protective vaccination against yellow fever and smallpox through the slightly scarified skin. The mixed vaccine, composed of mouse-fixed neurotropic virus and vaccinal virus prepared according to H. Plotz after a trial on rhesus monkeys and then on volunteers, 4 white and 2 black, had been given to 741 persons without any bad results, and conferred immunity to yellow fever in 90 per cent, and to smallpox in the same proportion as in ordinary Jennerian vaccination. A double protection could thus be given to very large numbers of natives, for example of French East Africa, who otherwise served as a reservoir of yellow fever infection.

Peltier, M., Durieux, C., Jonchère, H., and Arque, I. (1939) *Bull. Acad. Méd. Paris*, **121**, 657.

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